Chem. Pharm. Bull.
16(8)1608—1610(1968)

UDC 581.19 : 582.949.2 : 547.597.02

# Structure of Pogostol[1]

Hiroshi Hikino, Kunio Ito,
and Tsunematsu Takemoto

*Pharmaceutical Institute, School of Medicine, Tohoku University*[2]

(Received December 19, 1967)

From patchouli oil, obtained from patchouli, *Pogostemon cablin* (Labiatae), has been isolated a new sesquiterpenic alcohol, pogostol, of the formula $C_{15}H_{26}O$, whose structure has been established as shown in formula I on the basis of chemical and physico-chemical data.

Patchouli, *Pogostemon cablin* Benthum (Labiatae), is a perennial plant native to the Philippines, and cultivated in tropical Asia for patchouli oil, an important material in the perfumary industry. The constituents of patchouli oil has frequently been investigated, and the presence of a number of sesquiterpenoids have been reported.[3] In our work we have isolated a new sesquiterpenic alcohol for which the name pogostol is proposed. The present paper provides evidence which indicates that pogostol has the structure I.

Pogostol has the molecular formula $C_{15}H_{26}O$. The spectral properties show the presence of a tertiary hydroxyl (3420 $cm^{-1}$), a secondary methyl (9.13$\tau$), a tertiary methyl (8.88$\tau$), and an isopropenyl group (3072, 1643, 880 $cm^{-1}$, 8.34, and 5.42$\tau$). That pogostol contains only one double bond was verified by its hydrogenation to yield the saturated dihydro-derivative (II). The presence of the above functional groups and the molecular formula require that pogostol be a bicarbocyclic substance. The carbon skeleton of pogostol was clarified by its dehydrogenation giving S-guaiazulene (III), an observation which indicates that pogostol has the guaiane skeleton. Therefore, the tertiary hydroxyl group must be located at C-4 or C-10, since the nuclear magnetic resonance (NMR) spectrum of pogostol demonstrates that one of the methyl groups is tertiary and attached to a hydroxyl-bearing carbon. In order to settle this problem, *i.e.*, the orientation of the hydroxyl group, dihydropogostol (II) was treated with phosphorus oxychloride in pyridine affording the monounsaturated hydrocarbon (IV) whose infrared and NMR spectra exhibit the absence of the hydroxyl group and the tertiary methyl group, observed in the spectra of dihydropogostol (II), and instead the presence of a vinyl methyl group (8.39$\tau$). Since no vinyl hydrogen signal is visible, the newly formed ethylene bond is, therefore, tetrasubstituted. Ozonolysis of the monoene (IV) yielded the diketone (V), the infrared and NMR spectra of which revealed the formation of an acetyl (1716 $cm^{-1}$ and 7.95$\tau$) and a cyclopentanone (1735 $cm^{-1}$). This finding excludes the situation of the ethylenic linkage at C-4:C-5 in the monoene (IV), and consequently the location of the hydroxyl at C-4 in pogostol. It follows that the double bond in the monoene (IV) is located at C-1:C-10, and the hydroxyl group in pogostol is, therefore, situated at C-10. This assignment was further confirmed by the following series of reactions. Thus the dione (V) was subjected to aldol condensation. However, the product was not the expected enone (VI) but the $\beta$-ketol (VII) whose structure was deduced by its spectral data that show the presence of a chelated acetyl group (1691 $cm^{-1}$ and 7.88$\tau$) and a chelated tertiary hydroxyl group (3520 $cm^{-1}$) as well as three secondary methyl groups (9.12, 9.12, and 9.05$\tau$).

---

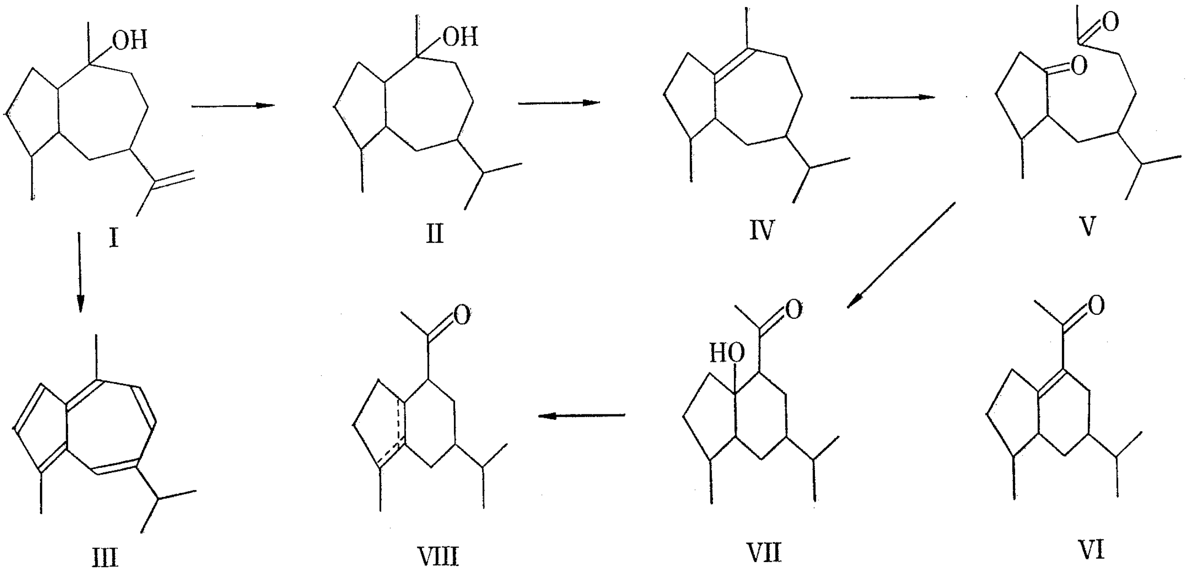
[1] This paper is Part XXVII in the series on Sesquiterpenoids. Preceding paper, Part XXVI: H. Hikino, Y. Sakurai, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **16**, 1605 (1968).

[2] Location: *Kita-4-bancho, Sendai.*

[3] For a historical background of early works, see E. Gildemeister and F. Hoffmann, "Die Ätherischen Öle," Vol. VII, Akademie Verlag, Berlin, 1961, p. 449.

Treatment of the $\beta$-ketol (VII) with phosphorus oxychloride in pyridine recovered the starting ketol (VII), while treatment with dil. sulfuric acid gave a dehydration product which, however, was again not the enone (VI) but a mixture of two hydrocarbons (VIII) judging by inspection of its NMR spectrum.

Based on the above evidence, the structure of pogostol is shown as formula I.



### Experimental[4]

**Isolation of Pogostol**——Patchouli oil (50 g) was chromatographed over alumina (700 g). Benzene eluate (7.5 g) was rechromatographed over silica gel (250 g). Elution with light petroleum—benzene (1:1) and distillation under reduced pressure gave pogostol (I) as a colorless oil (5.0 g), $[\alpha]_D$ $-20.2°$ ($c$=8.7). *Anal.* Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.73; H, 11.56. IR (liquid) $cm^{-1}$: 3420 (hydroxyl), 3072, 1643, 880 (vinylidene), NMR: doublet (3H) at 9.13 $\tau$ ($J$=6, $C_{(14)}H_3$), singlet (3H) at 8.88 $\tau$ ($C_{(15)}H_3$), singlet (3H) at 8.34 $\tau$ ($C_{(13)}H_3$), single peak (2H) at 5.42 $\tau$ ($C_{(12)}H_2$).

**Hydrogenation of Pogostol over Adams' Catalyst in Methanol**——Pogostol (164 mg) in MeOH (5 ml) was hydrogenated over $PtO_2$ (15 mg). After the uptake of $H_2$ (1 mole), the mixture was worked up in the usual way and distilled under diminished pressure yielding dihydropogostol (II) as a colorless oil (159 mg), $[\alpha]_D$ $-29.9°$ ($c$=4.3). *Anal.* Calcd. for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.59; H, 12.41. IR ($CCl_4$) $cm^{-1}$: 3630, 3420 (hydroxyl), NMR: doublet (6H) at 9.17 $\tau$ ($J$=6, $C_{(12)}H_3$, $C_{(13)}H_3$), doublet (3H) at 9.08 $\tau$ ($J$=5, $C_{(14)}H_3$), singlet (3H) at 8.91 $\tau$ ($C_{(15)}H_3$).

**Dehydrogenation of Pogostol with Palladium Carbon**——Pogostol (50 mg) and Pd-C (10%; 25 mg) were heated at 320—325° for 3 min. The product in light petroleum was chromatographed over alumina (1 g). Elution with the same solvent gave S-guaiazulene (III) as a blue oil, UV $\lambda_{max}^{EtOH}$ m$\mu$: 243, 284, 288 (inflection), 303, 348, 365, *ca.* 600. The identity was confirmed by the usual criteria.

**Dehydration of Dihydropogostol with Phosphorus Oxychloride in Pyridine**——Dihydropogostol (II) (1.0 g) in pyridine (7 ml) was treated with $POCl_3$ (3 ml) at 0° overnight. Upon isolation, the product was distilled under reduced pressur give anhydrodihydropogostol (IV) as a colorless oil (924 mg), $[\alpha]_D$ $-11.5°$ ($c$=5.9). NMR: doublet (6H) at 9.17 $\tau$ ($J$=6, $C_{(12)}H_3$, $C_{(13)}H_3$), doublet (3H) at 9.13 $\tau$ ($J$=6, $C_{(14)}H_3$), singlet (3H) at 8.39 $\tau$ ($C_{(15)}H_3$).

**Ozonolysis of Anhydrodihydropogostol**——The monounsaturated hydrocarbon (IV) (367 mg) in AcOEt (7 ml) was ozonized at 5°. The mixture was hydrogenated over $PtO_2$ (20 mg), and worked up in the usual manner. The product (358 mg) was chromatographed over silica gel (10 g). Elution with benzene and distillaltion under diminished presssure afforded the diketone (V) as a colorless oil (159 mg), $[\alpha]_D$ $+23.9°$ ($c$=6.2). *Anal.* Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.34; H, 10.78. IR ($CCl_4$) $cm^{-1}$: 1735 (cyclopentanone), 1716 (acetyl), 1408 (methylene $\alpha$ to carbonyl). NMR: doublet (3H) at 9.17 $\tau$ ($J$=6, $C_{(14)}H_3$), doublet (6H) at 9.15 $\tau$ ($J$=6, $C_{(12)}H_3$, $C_{(13)}H_3$), singlet (3H) at 7.95 $\tau$ ($C_{(15)}H_3$).

---

[4] Specific rotations were measured in $CHCl_3$ solution. NMR spectra were determined at 60 Mcps in $CCl_4$ solution *vs.* $Me_4Si$ as internal reference. Chemical shifts are given in $\tau$-units and coupling constants ($J$) in cps.

**Aldol Condensation of the Diketone**——The dione (V) (150 mg) and NaOH (0.2 g) in MeOH (5 ml) were let standing at room temperature for 1 hr. After work-up in the usual way, the product (127 mg) was distilled under reduced pressure yielding the keto-alcohol (VII) as a colorless oil, $[\alpha]_D$ $-39.0°$ ($c=4.0$). *Anal.* Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 74.84; H, 10.98. IR ($CCl_4$) $cm^{-1}$: 3520 (chelated hydroxyl), 1691 (chelated acetyl), NMR: doublet (6H) at 9.12 $\tau$ ($J=6$, $C_{(12)}H_3$, $C_{(13)}H_3$), doublet (3H) at 9.05 $\tau$ ($J=6$, $C_{(14)}H_3$), singlet (3H) at 7.88 $\tau$ ($C_{(15)}H_3$).

**Attempted Dehydration of the Ketol with Phosphorus Oxychloride in Pyridine**——The ketol (VII) (60 mg) in pyridine (1 ml) was allowed to stand with $POCl_3$ (0.1 ml) at 0° for 2 days. The mixture was worked up as usual. The product (60 mg) was identified with the starting ketol (VII) in the customary criteria.

**Dehydration of the Ketol with dil. Sulfuric Acid**——The ketol (VII) (70 mg) was heated with $H_2SO_4$ (5%; 2 ml) at 100° for 5 hr. Ether extraction gave the product (60 mg) which was chromatographed over silica gel (2 g). Light petroleum-benzene (1:1) eluate (36 mg) was distilled under reduced pressure to yield the mixture of the unsaturated methyl ketone (VIII) as a colorless oil, IR ($CCl_4$) $cm^{-1}$: 1706 (acetyl), NMR: doublet (6H) at 9.08 $\tau$ ($J=6$, $C_{(12)}H_3$, $C_{(13)}H_3$), doublet (~1H) at 8.99 $\tau$ ($J=6$), unresolved singlet (~2H) at 8.42 $\tau$ ($C_{(14)}H_3$), two singlets (3H) at 8.03, 7.96 $\tau$ ($C_{(15)}H_3$).

**Acknowledgement** Thanks are due to Analytical Laboratories, this Institute, for microanalyses and NMR measurements.