[Chem. Pharm. Bull.
13(12)1484~1485(1965)]

UDC 581.19 : 582.572.4 : 547.597

Structure of Curcumol

From the rhizome of zedoary (*Curcuma zedoaria* Roscoe) a new sesquiterpenoid hemiketal, $C_{15}H_{24}O_2$, m.p. 141~142°, $[\alpha]_D$ −40.8°,[*1] has been isolated for which the name curcumol is proposed. The authors now wish to report evidence which leads to the expression I (R=H) for this substance.

The presence of one vinylidene group in curcumol as its only element of unsaturation [IR bands (KBr) at 1645, 882 cm^{-1}, NMR ($CDCl_3$) 2H triplet (J=1.5) at 5.15 τ] was confirmed by oxidation with perbenzoic acid to two epimeric monoepoxides (II), the epoxide A, $C_{15}H_{24}O_3$, m.p. 129.5~131°, $[\alpha]_D$ −42.4°, and the epoxide B, $C_{15}H_{24}O_3$, m.p. 109~110.5°, $[\alpha]_D$ −48.6°, and by hydrogenation to the saturated dihydro-derivative (III) (*vide infra*).

The nature of the oxygen functions was revealed as follows. Curcumol [IR band (KBr) at 3420 cm^{-1} (hydroxyl), NMR ($CDCl_3$) 1H singlet at 7.25 τ ($\text{-O}\underline{\text{H}}$)] formed the monoapetate (I; R=Ac), $C_{17}H_{26}O_3$, n_D^{25} 1.482, $[\alpha]_D$ −23.3°, IR bands at 1757, 1214 cm^{-1} (acetoxyl), NMR 3H singlet at 8.06 τ ($\text{C}\underline{\text{H}}_3\text{-CO-O-}$). Curcumol was transformed by methanolic and ethanolic hydrochloric acid into the corresponding ethers : the methyl ether (I; R=CH_3), $C_{16}H_{26}O_2$, n_D^{25} 1.483, $[\alpha]_D$ +8.3°, NMR 3H singlet at 6.75 τ ($\text{C}\underline{\text{H}}_3\text{-O-}$), and the ethyl ether (I; R=C_2H_5), $C_{17}H_{28}O_2$, n_D^{25} 1.479, $[\alpha]_D$ −18.3°, NMR 3H triplet (J=7.1) at 8.66 τ ($\text{C}\underline{\text{H}}_3\text{-CH}_2\text{-O-}$), two 1H quartets (J=7.1) at 6.42 and 6.37 τ ($\text{CH}_3\text{-C}\underline{\text{H}}_2\text{-O-}$). On acid treatment in aqueous acetone both the ethers reverted to curcumol. Lithium aluminum hydride reduction of curcumol gave the two epimeric diols (IV) : the diol A, $C_{15}H_{26}O_2$, n_D^{25} 1.505, $[\alpha]_D$ −5.9°, NMR 1H triplet (J=3.9) at 5.99 τ ($\text{HO-C}\underline{\text{H}}\langle$), and the diol B, $C_{15}H_{26}O_2$, m.p. 78~79°, $[\alpha]_D$ +3.2°, NMR 1H doublet (J=5.0, unresolved) at 6.23 τ ($\text{HO-C}\underline{\text{H}}\langle$). Oxidation of both the diols with chromic acid regenerated curcumol. The combined evidence points to a hemiketal structure for curcumol. The nuclear magnetic resonance spectra of curcumol and its derivatives lack a hydrogen signal of the $\underline{\text{H}}\text{-C-O-}$ type ; this indicates the hindered hydroxyl group of curcumol to be tertiary.

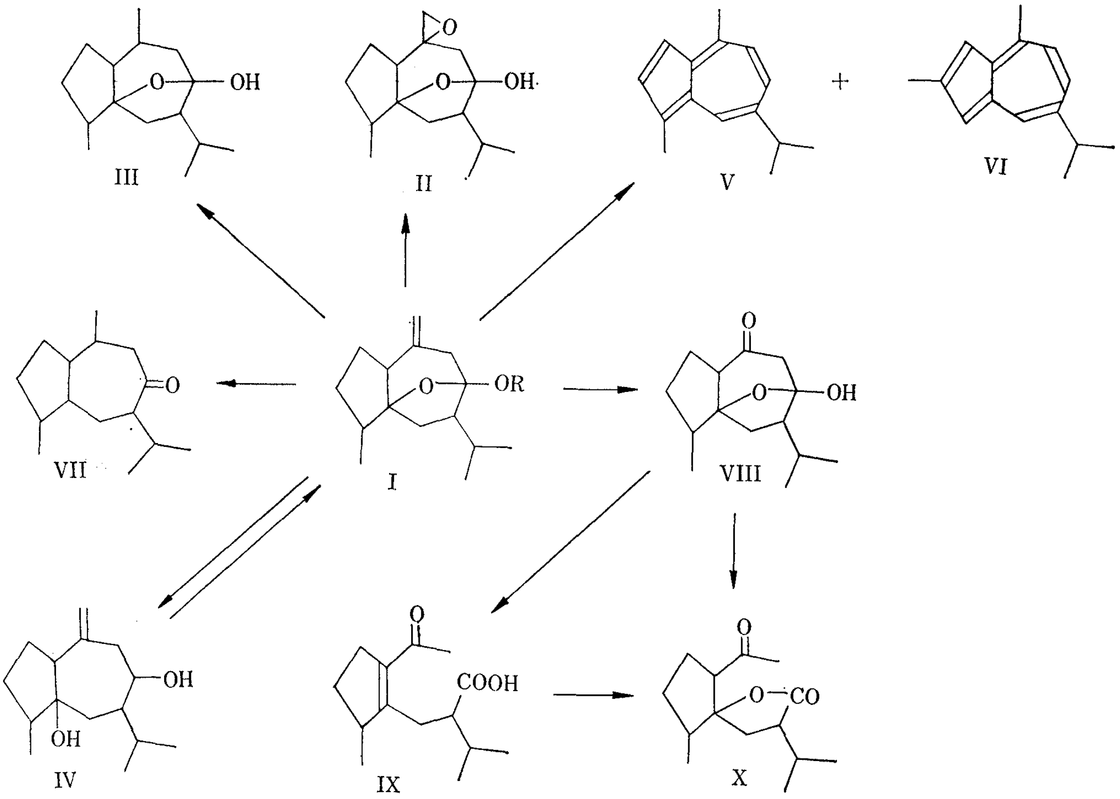
Dehydrogenation of curcumol with palladized charcoal gave S-guaiazulene (V)[1,3,5-trinitrobenzene adduct : m.p. 145°] together with a small amount of Se-guaiazulene (VI) [1,3,5-trinitrobenzene adduct : m.p. 140°]. Consistent with this guaiane skeleton, the nuclear magnetic resonance spectra of curcumol and its derivatives show the presence of a vinylidene or equivalent, secondary methyl, and an isopropyl group.

Hydrogenation of curcumol over Adams' catalyst in methanol afforded the dihydro-derivative (III), $C_{15}H_{26}O_2$, m.p. 102~104°, $[\alpha]_D$ +5.2°, IR band (KBr) at 3390 cm^{-1} (hydroxyl). Whilst on hydrogenation of curcumol over palladized charcoal (freshly prepared from palladium chloride by hydrogenation) in methanol yielded the ketone (VII), mol. wt. 222 (mass spec.), $C_{15}H_{26}O$, n_D^{25} 1.477, $[\alpha]_D$ −39.9°, IR band at 1704 cm^{-1} (carbonyl in a six-membered or larger ring). On base-catalyzed deuteration the ketone (VII) gave the trideuterio-derivative, mol. wt. 225 (mass spec.), IR band at 1692 cm^{-1}, indicating the location of the carbonyl at C-8 or C-9 on the guaiane skeleton.

Curcumol was ozonized to yield the keto-hemiketal (VIII), NMR 2H singlet at 7.40 τ ($\text{-CO-C}\underline{\text{H}}_2\text{-C(OH)-O-}$), whose carbonyl absorption in the infrared appeared at 1704 cm^{-1}

[*1] Analytical values are in accord with the molecular formulae shown. $[\alpha]_D$s refer to $CHCl_3$ solution and IR spectra to liquid film unless otherwise indicated. NMR spectra were determined at 60 Mc. in CCl_4 solution against internal $(CH_3)_4Si$ unless specified to the contrary. Chemical shifts are given in τ-values and coupling constants (J) in c.p.s.

showing the size of the ring as six or larger. This defines the orientation of the vinylidene group at C-10 and also the attachment of the hemiketal linkage at C-5 and C-8 in curcumol which, therefore, is represented by structure I (R=H).



This assignment was confirmed by the following two series of experiments.

Alkali treatment of the keto-hemiketal (VIII) gave the unsaturated keto-acid (IX; R=H) which was characterized as the methyl ester (IX; R=CH_3), $C_{15}H_{24}O_3$, mol. wt. 252 (mass spec.), n_D^{25} 1.478, $[\alpha]_D$ −196.2°, UV λ_{max}^{EtOH} 257 mμ (log ε 3.67), IR bands at 1736 (ester), 1678, 1605 cm^{-1} (conjugated enone), NMR 3H singlet at 7.89 τ ($C\underline{H}_3$-CO-), 3H singlet at 6.43 τ ($C\underline{H}_3$-O-CO-), iodoform test: positive. This transformation show the carbonyl in the keto-hemiketal (VIII) to be situated in the β and β' positions of the carbons which participate to form the hemiketal linkage.

The keto-hemiketal (VIII), when heated, gave the keto-lactone (X), $C_{14}H_{22}O_3$, n_D^{25} 1.470, $[\alpha]_D$ +12.6°, which was also obtained from the keto-acid (IX; R=H) on standing. The spectra of the keto-lactone (X) showed the presence of an acetyl group (IR band at 1709 cm^{-1}, NMR 3H singlet at 7.92 τ) and a γ-lactone system (IR band at 1764 cm^{-1}) but no hydrogen of the $\underline{H}$-C-O- type. This verified the situation of the masked hydroxyl in curcumol at C-5.

The authors would like to express their thanks to Mr. H. Takahashi for the preliminary experiments, to Research Laboratories, Takeda Chemical Industries, Ltd., for the nuclear magnetic resonance spectra, and to Hitachi, Ltd., for the mass spectra.

Pharmaceutical Institute,
School of Medicine,
Tohoku University,
Kita-4-bancho, Sendai

Hiroshi Hikino (ヒキノヒロシ)
Kanji Meguro (目黒寛司)
Yojiro Sakurai (桜井洋二郎)
Tsunematsu Takemoto (竹本常松)

Received September 28, 1965