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THE CONVERSION OF PODOCARPIC ACID TO NIMBIOL

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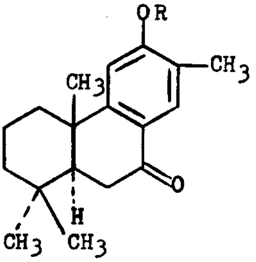
NIMBIOL[1], a compound isolated from the trunk bark of Melia azadirachta Linn., has been assigned[2-3] the structure Ia.



Ia. R=H

b. R=CH_3

We have converted podocarpic acid to compounds having structures Ia and Ib and have found them to be identical with nimbiol and nimbiol methyl ether[1] thus confirming the complete structures assigned[3] by Choudhuri, Khastgir and Sengupta.

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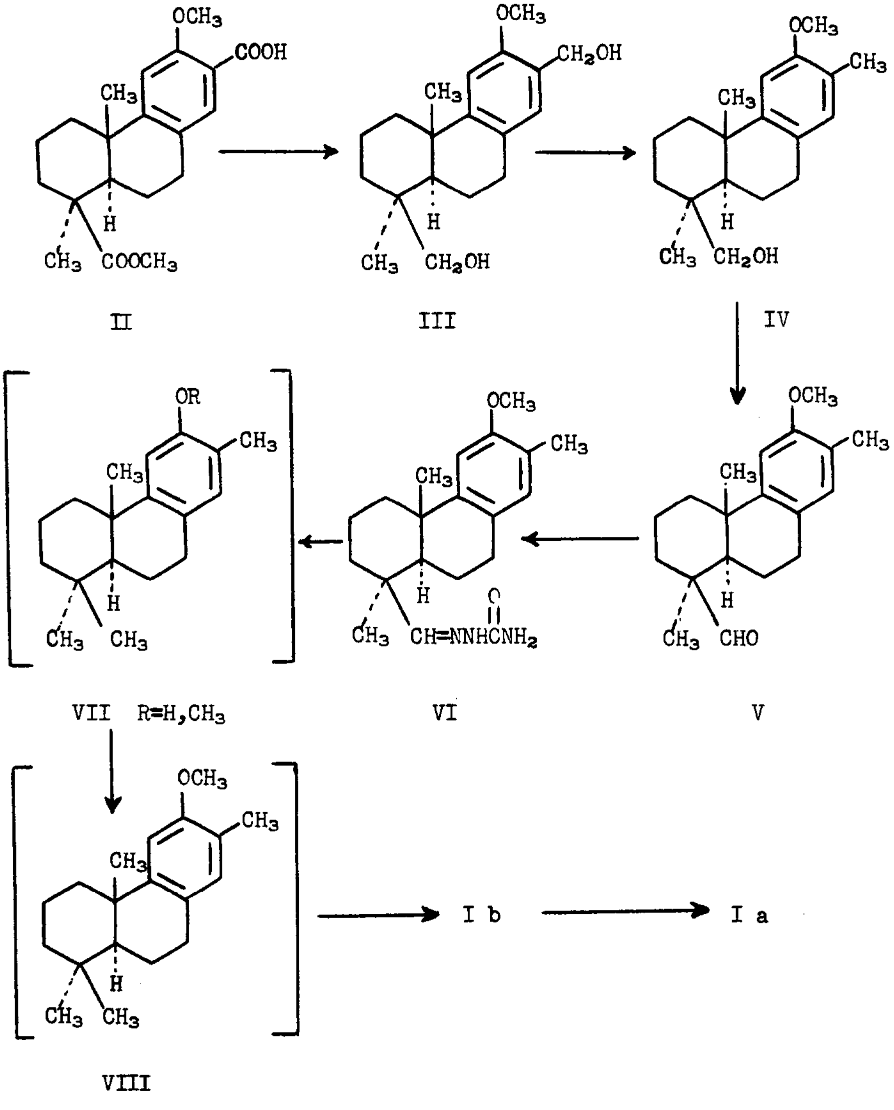
[1] P. Sengupta, S. N. Choudhuri and H. N. Khastgir, Chem. and Ind. 861 (1958).

[2] S. N. Choudhuri, H. N. Khastgir and P. Sengupta, Chem. and Ind. 634 (1959).

[3] S. N. Choudhuri, H. N. Khastgir and P. Sengupta, Chem. and Ind. 1284 (1959).



II
III
IV
V
VI
VII R=H,CH3
VIII
I b
I a
OCH3
COOH
CH2OH
CH3
COOCH3
CHO
CH=NNHCNH2
OR
H

Methyl O-methyl-7-carboxypodocarpate[4] (II) was reduced with lithium aluminum hydride in tetrahydrofuran to the glycol III; m.p. 119.5-122°; $[\alpha]_D$ +69°[5]; λ_{max}^{MeOH} 280 (log ϵ = 3.46) and 285mμ (log ϵ = 3.46). (Found: C,74.94; H, 9.19. $C_{19}H_{28}O_3$ requires: C, 74.96; H, 9.27%). Hydrogenolysis of III over palladium-charcoal in the presence of hydrochloric acid gave IV; m.p. 83-85°; $[\alpha]_D$ +68°; λ_{max}^{MeOH} 280 (log ϵ = 3.47) and 287 mμ (log ϵ = 3.47). (Found: C, 79.11; H, 9.94. $C_{19}H_{28}O_2$ requires: C, 79.12; H, 9.79). Oxidation of IV with chromic acid-sulfuric acid in acetone gave the aldehyde, V; m.p. 110-111.5°; $[\alpha]_D$ +87°; λ_{max}^{MeOH} 281 (log ϵ = 3.49) and 286 mμ (log ϵ = 3.48). (Found: C, 79.44; H, 9.34. $C_{19}H_{26}O_2$ requires: C, 79.68; H, 9.15). The aldehyde V was converted to the semicarbazone VI; m.p. 210-212°; λ_{max}^{MeOH} 280 (log ϵ = 3.52) and 286mμ (log ϵ = 3.49). (Found: C, 69.88; H, 8.38. $C_{20}H_{29}N_3O_2$ requires: C, 69.94; H, 8.51%). The semicarbazone (VI) was heated at 200° with sodium ethoxide in ethanol. The crude product (VII) was subjected to remethylation with dimethyl sulfate and sodium hydroxide followed by an oxidation with chromic acid in aqueous acetic acid to give Ib; m.p. 142-144°; $[\alpha]_D$ +43°; λ_{max}^{EtOH} 230 (log ϵ = 4.16) and 277 mμ (log ϵ = 4.12). This product was identical (no depression of the melting point on admixture; identical infrared absorption spectra at 5% in chloroform; identical ultraviolet spectra) with nimbiol methyl ether (reported[1]: m.p. 142-143°; $[\alpha]$ +43.7°). Demethylation of Ib with pyridine hydrochloride

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[4] G. M. Picha, U. S. Patent 2,767,162 (1956).

[5] All rotations were determined using 1% solutions in chloroform.

gave the free phenol Ia; m.p. 248-252°; $[\alpha]_D$ +33°; λ_{max}^{EtOH} 234 ($\log \epsilon$ = 4.13) and 283 $m\mu$ ($\log \epsilon$ = 4.10); $\lambda_{max}^{0.1\ N\ NaOH/EtOH}$ 253 ($\log \epsilon$ = 3.84) and 345 $m\mu$ ($\log \epsilon$ = 4.38) [reported[1,2]: m.p. 244°; $[\alpha]_D$ +32.3°; λ_{max}^{EtOH} 231 ($\log \epsilon$ = 4.07) and 286 $m\mu$ ($\log \epsilon$ = 4.06); $\lambda_{max}^{0.1\ N\ NaOH/EtOH}$ 251 ($\log \epsilon$ = 3.89) and 344 $m\mu$ ($\log \epsilon$ = 4.33)]. Remethylation of this phenol (Ia) gave the original methyl ether (Ib).

We are highly indebted to Dr. P. Sengupta of the East India Pharmaceutical Works Ltd., Calcutta-34, India for the gift of the nimbiol methyl ether.