Aus diesen Werten geht hervor, dass im Laufe der Dehydrierung sowohl aus C-2 als auch aus C-3 des Eduktes spezifisch das H_R-Atom abgespalten wird, entsprechend einer *trans*-Abspaltung von H-Atomen aus jener antiperiplanaren Konformation des Substrates (vergleiche **2**), welche der fixierten *trans*-Anordnung des Produktes topologisch am nächsten steht. Die Verhältnisse sind besonders klar bei den Tritiobuttersäuren **7** und **9**, welche aus enzymatisch dargestellten chiralen [1-^{3}H]-Propanolen erhalten worden waren und die bei der Oxydation entweder alles oder kein Tritium verloren (Experiment Nr. 1 und 3). Retention bzw. Verlust von Tritium sind hingegen nicht so vollständig bei der Oxydation von Verbindungen **14** und **17** (Experiment Nr. 4, 5, 6 und 7). Der Grund dafür dürfte eher in der geringeren sterischen Reinheit der Substrate als in einer mangelnden Stereospezifität des Enzyms zu suchen sein. Hinsichtlich des sterischen Verlaufs der Reaktion bestehen somit für den hier untersuchten Vorgang ähnliche Verhältnisse wie bei der enzymatischen Dehydrierung von Bernsteinsäure[2].

Übereinstimmende Resultate sind inzwischen in unabhängigen Untersuchungen mit dem gleichen Enzym von DRYSDALE[14] erzielt worden. In die gleiche Richtung weisen ferner die Experimente von SIMON et al.[15] über die Bildung von Buttersäure in *Clostridium tyrobutyricum*[15] und in *Clostridium kluyveri*[16].

Summary. The stereochemistry of the formation of crotonyl CoA from butyryl CoA catalyzed by the appropriate pig liver enzyme was investigated using samples of butyric acid specifically labelled with tritium in the two methylene groups. It is shown that oxidation involves specific removal of the pro-R hydrogen atoms from positions 2 and 3 of the substrate.

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Demethylcephaeline, a New Alkaloid from *Alangium lamarckii*. Characterization of AL 60, the Hypotensive Principle from the Stem-Bark

A number of alkaloids possessing isoquinoline and its hybrid structures with β-carboline have been isolated from the seeds[1], roots[2], leaves[3] and fruits[4] of *Alangium lamarckii* Thw. (Alangiaceae). We report the isolation of yet another new alkaloid and characterization of an amorphous drug, designated as AL 60, from the stem-bark of the same plant. The latter, showing a low toxicity and insignificant side effects[5], was found to exert interesting biphasic action on blood pressure of cats injected i.v. under either chloralose-urethane or sodium nembutal anaesthesia. The actions were dose-dependent, sustained and prolonged.

The total crude alkaloid mixture from the stem-bark was chromatographed over silica gel. Elution with chloroform containing increasing proportions (0.5–10%) of methanol yielded cephaeline, $[\alpha]_D$ — 39.6° ($CHCl_3$), characterized as hydrochloride, mp 254–257°, $[\alpha]_D$ + 21° (H_2O); psychotrine, mp 121–123°, $[\alpha]_D$ + 80.2° (MeOH), M^+ at *m/e* 464, dihydrogen oxalate, mp 131–145°, $[\alpha]_D$ + 21.6° (H_2O); tubulosine, mp 257°, $[\alpha]_D$ — 73.0° (C_5H_5N); desmethylpsychotrine[2], mp 165–167°, $[\alpha]_D$ + 72.3° (MeOH) and a new amorphous base, mp 147–149°, $[\alpha]_D$ — 53.5° ($CHCl_3$). The last one was eluted with 5% methanol in chloroform and purified through preparative TLC on silica gel using a mixture of benzene-ethyl acetate-diethylamine (2:2:1) as the developing solvent.

The new base formed a hydrochloride, mp 262–265° (dec.) $[\alpha]_D$ + 19.8° (H_2O). On treatment with diazomethane and following the conversion by TLC, it was observed that the compound formed cephaeline (Ic) within 5 min, while emetine (Id), which could be detected after 1 h, was the major product after 24 h. The mass spectrum[6] of the alkaloid exhibited molecular ion at *m/e* 452 corresponding to the molecular formula $C_{27}H_{36}N_2O_4$ and the base peak at *m/e* 178. The fragmentation pattern was found to be exactly parallel to that of cephaeline, except that the ion peaks corresponding to the A/B/C ring system were shifted to lower values by 14 mass units (at *m/e* 274, 272, 260, 259, 258, 232, 230, 192 and 191). The compound could thus be inferred to be a ring A monodemethylated cephaeline.

Its IR-spectrum in Nujol exhibited a broad peak of medium intensity between 9.7–9.9 μ as against two sharp ones in that of cephaeline in the same region, for =C–O–C symmetrical stretching vibration, similar to the observed difference between the spectra of desmethylpsychotrine and psychotrine.

The UV-absorptions of the compound, λ_{max} (log ε) at 211 (4.28), 225 s (3.91) and 286 (3.69) nm in ethanol and at 213 s (3.48), 227 (3.96), 247 (4.05) and 301 (3.81) nm in 0.1 *N* alcohol. NaOH were very close to those of cephaeline with the difference that the bathochromic shift of the peak at 285 nm in alkaline medium was complete only in the former. This observation is compatible with the presence of a phenolic hydroxy group also in ring A of the new base, though it did not permit a discrimination between its location either at position 6 or 7. The compound was, however, found to be identical (IR) with the major product obtained by demethylation of cephae-

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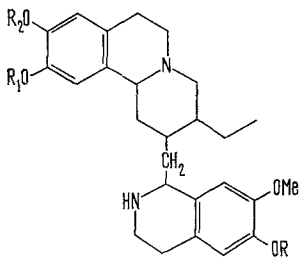
line with 1:1 hydrochloric acid under reflux. The alternative structure Ia or Ib is therefore assigned to the new base with our preference for Ia because of the expected preferential demethylation at the electron-rich position 7 rather than at 6.

AL 60, mp 160–162°, $[\alpha]_D \pm 0°$ ($CHCl_3$), was previously isolated[5] from the chloroform solution of the total crude bases by repeated and successive removal of impurities by dilution with ether, concentration and precipitation with light petroleum. It was subsequently proved to be a mixture of at least 3 components by TLC over silica gel using chloroform:methanol (85:15) as developing solvent.

After several chromatographic separations and crystallisations, the constituents[7] were eventually identified as psychotrine, cephaeline and demethylcephaeline. The



Ia, R=R1=H, R2=Me
b, R=R2=H, R1=Me
c, R=H, R1=R2=Me
d, R=R1=R2=Me

reason why they eluded detection so far was that the almost zero specific rotation recorded in the presence of adhering impurity which was too difficult to remove misled us to assume the compounds to be racemic in nature. However, to the best of our knowledge, no work has so far been reported on the effect of the constituents of AL 60 on blood pressure though scanty reports are traceable on such effect of emetine[8] and *O*-methylpsychotrine[9].

Résumé. A partir de l'écorce de la tige d'*Alangium lamarckii* Thw., une base, $C_{27}H_{36}N_2O_4$ (p.f. 147–149°, $[\alpha]_D - 53,5°$) ainsi que de la céphaeline, psychotrine, desméthylpsychotrine et tubulosine ont été isolées. Cette nouvelle base est identifiée comme déméthylcéphaeline, montrant que le principe hypotendu AL 60, précédemment obtenu de la même provenance est un mélange de psychotrine, de céphaeline et de déméthylcéphaeline.

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Indian Institute of Experimental Medicine, Calcutta 32 (India), 9 March 1970.

[7] The proportions of psychotrine and cephaeline, the major constituents, varied somewhat on the extent of preliminary purification.

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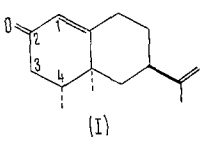
Conformation of Nootkatone

Nootkatone, originally isolated from a heartwood of *Chamaecyparis nootkatensis*, was reported[1] to exhibit $[\alpha]_D + 195.5°$. The same ketone was isolated from *Citrus paradisi* and the structure was confirmed as (I) on the basis of IR- and NMR-spectra, ORD curve and chemical degradation[2]. The total synthesis of (I) was recently



(I)

accomplished[3,4]. We have now attempted to clarify the preferred conformation of nootkatone by a combination of CD curve and NMR-spectrum measurements at various temperature.

Nootkatone (I) may take 3 possible conformations: Ia, Ib and Ic, as shown in Figure 1. The back octant rule is applied to transoid α,β-unsaturated ketone, and the sign of the Cotton effect is predicted from the octant

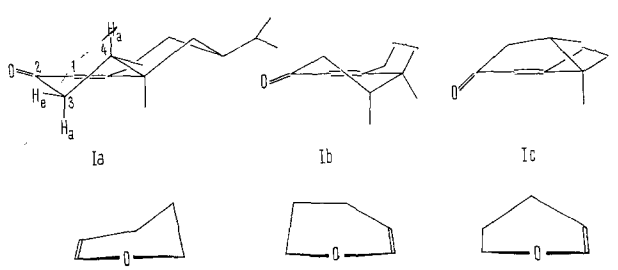


Fig. 1. Possible conformations of nootkatone and the octant projection diagram.

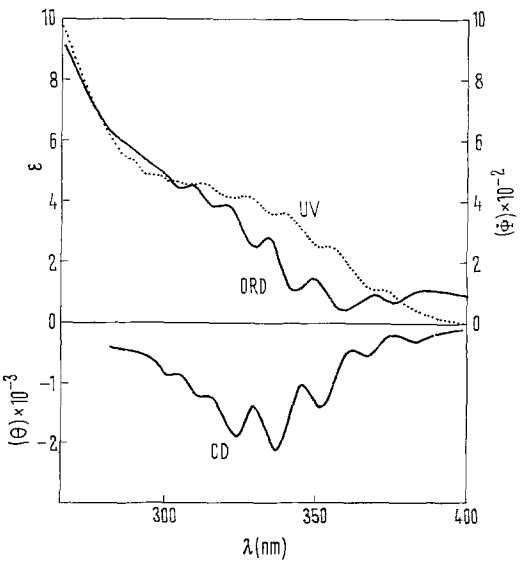


Fig. 2. ORD, UV- and CD-curves of nootkatone in isooctane at 25 °C.