We find (C)Me 5-78, 6-37 %; active H, 0-62 % [2(C)Me requires 7-7 and 2 H requires 0-52 %].

The I.R. absorption spectrum includes bands at 2-82, 3-00 and 3-28 μ (OH and NH), 5-86 μ and 5-94 μ (ester or ketone carboxyl group conjugated with a double bond), 6-14 μ (asymmetrically substituted double bond) and 13-30 μ (o-disubstituted benzene nucleus). This evidence, together with the U.V. is consistent with the presence of MeO=C—C=O—, although the extra conjugated carboxyl peak in the I.R. is an unusual feature. There is an "extra" carbon atom, probably corresponding to a (C)Me, and the constitution (V) is feasible (R = H, R' = Me, or R = Me, R' = H), this structure also showing the suggested 1 relation to mayumbine.

Akuammiline (C19H20O4N2) is said to contain 10Me and no NMe. It appears to contain two (C)Me groups (7-0 %, theory, 7-9-9 %), and its U.V. spectrum is in the main like that of an indole, although it presents some slight variations. The first maximum at 2,200 A (log e, 4-23) is about 50 A shorter, and the second maximum at 2,9 μ (OH or NH or not significant), bands at 5-76 μ (C = O of unconjugated ester type), at 6-16 μ (probably C = C but could be C = N), at 6-26 μ (more conjugated C = C), at 13-29 μ (o-disubstituted benzene, but this is uncertain because bands at 12-90 and 13-21 μ are also observed).

Akuammiline could be a keto-akuammigine or a hydroxydehydroakuammigine. The modified indole spectrum suggests that a functional group is attached to the indole nucleus. The base gives a bright crimson red OTTO reaction which is characteristic. The base gives a bright crimson red OTTO reaction which is characteristic.

Akuammicine (C22H24O41N2T2) contains 1 Me and no NMe. It contains the part structure —N—CO—C=C—, with an amide carbonyl, probably with further conjugation, 6-24 μ (probably armo tic double bond), 13-39 μ (o-disubstituted benzene, supported by absence of bands at 12-3 and 12-8 μ).

In the case of echitamidine 4 about half of the methyl was obtained as OMe (ZIESSL) and half as NM2 (HERZIG-MEYER), but there is only one methyl group, and hence the (O)Me is unusually hard to remove, or the (N)Me is unusually labile. We prefer the latter hypothesis, which was noted by GOODSON as a possibility, because COOMe cannot be present in akuammicine and it is hard to accommodate a methoxyl group otherwise.

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The Dyson Perrins Laboratory University of Oxford, December 17, 1952.

Zusammenfassung

Für das Alkaloid Akuammin wird die neue Brutto-

1 O. HASSEL et al., Acta Chem. Scand. I, 149, 929 (1947), and earlier papers.
3 D. H. R. BARTON, Exper. 6, 316 (1950).

The Origin of Steric Hindrance in Cyclohexane Derivatives

HASSEL 1 and PITZER 2 and coworkers have pointed out that in the stable or "chair" form of cyclohexane there are two types of bonds, so-called equatorial (κ or e) and polar (ε or p) bonds. On the basis of this concept, BARKTON 3 has been able to make important and far-reaching predictions on the reactivity of substituted cyclohexanes and natural products containing cyclohexane rings. One of these predictions is concerned with the relative ease of esterification of hydroxyl groups and ease of hydrolysis of ester groups in polar and equatorial positions. Hydroxyl groups are esterified more easily and ester groups hydrolyzed more easily when in the equatorial than when in the polar position, due to the greater steric hindrance in the latter. The reason for this might be twofold. It is possible that an ester group in the polar position of a substituted cyclohexane has to stay in this position during hydrolysis and that the resulting crowded transition state (crowded due to steric interference of non-adjacent polar substituents) accounts for the relatively slow rate (reaction path A). On the other hand, it is also possible that prior to reaction the molecule is forced into a different conformation in which the ester group is now in the equatorial position (and some other, more bulky group in the polar position), and that the slower rate is due to the extra energy required to bring about the conformational transformation (reaction path B).

1 O. HASSEL et al., Acta Chem. Scand. I, 149, 929 (1947), and earlier papers.
3 D. H. R. BARTON, Exper. 6, 316 (1950).
Fortunately data are already in the literature to permit one to distinguish between these two possibilities.

Presumably, the stable conformations of these molecules are such that the most bulky group (isopropyl) occupies an equatorial position\(^8\), as shown in the Table at the top. Barton\(^3\) has already pointed out that compounds having the hydroxyl group in the equatorial position in their most stable conformations are esterified faster than those having it in the polar position. Thus (I) and (II) are esterified faster than (III) and (IV). (II), which has a nonreactive substituent in the polar position reacts more slowly than (I) which has only equatorial substituents. However, if neoisomenthol and neomenthol reacted in their stable conformations—(III) and (IV)—one would expect (IV) to be esterified more rapidly than (III), since the former two alkyl groups (methyl and isopropyl) have to be forced into the crowded polar positions, in the latter only one (isopropyl). Therefore, making the reasonable assumption that (IIa) and (IVA) are of the same order of reactivity, (III) should be esterified more readily than (IV), which is in accordance with the experimental facts.

On the basis of this interpretation one would predict that cyclohexanols bearing a polar hydroxyl group in a rigid system which cannot change conformation so as to place the hydroxyl group in the equatorial position should show much greater difference in esterification and saponification rates (compared with their epimers with equatorial hydroxyl groups) than the more mobile molecules discussed above. Such rigid molecules are the trans-decalols (V) and trans-hydrindanols (VI) as well as the steroid alcohols. Quantitative data from the steroid field are not available, but qualitative observations\(^1\) point to a large difference in ease of esterification and hydrolysis between epimers. The decalols,

\[\begin{array}{|c|c|c|c|}
\hline
\text{Compound} & \text{k} & \text{k} \\
\hline
\text{trans-} \alpha \text{-decalol, Isomer I} & 0.0382 & 19.0 \\
\text{trans-} \alpha \text{-decalol, Isomer II} & 0.725 & 6.91 \\
\text{trans-} \beta \text{-decalol, Isomer I} & 0.470 & 1.77 \\
\text{trans-} \beta \text{-decalol, Isomer II} & 3.25 & 2.75 \\
\text{cis-} \alpha \text{-methylcyclohexanol} & 0.0199 & 6.91 \\
\text{cis-} \alpha \text{-methylcyclohexanol} & 0.0352 & 1.77 \\
\text{cis-} \alpha \text{-decalol, Isomer I} & 0.438 & 2.75 \\
\text{cis-} \alpha \text{-decalol, Isomer II} & 1.201 & 1.77 \\
\hline
\end{array}\]

\(^{1}\) L. F. Fieser, Exper. 6, 312 (1950).

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\(^{1}\) J. Read and W. J. Grubb, J. Chem. Soc. 1934, 1729.

\(^{2}\) W. Hückel et al., Ann. Chem. 533, 123 (1937).

\(^{3}\) D. H. R. Barton, Exper. 6, 316 (1950).