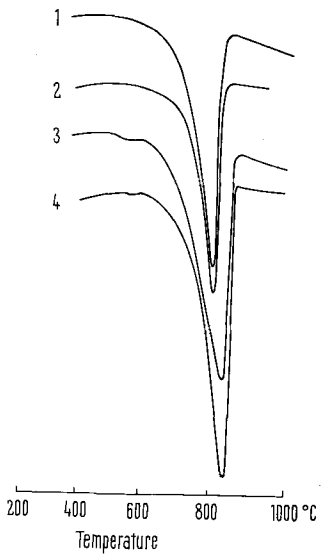

Differential thermal patterns for (1) pure synthetic calcite, (2) mixture of pure calcite with 20% pure dolomite, (3) magnesian calcite (synthetic with Ca_9Mg_1 composition) and (4) natural magnesian calcite.

magnesian calcite a shift in the dissociation to 830 °C is noticed. A similar shift to 842 °C is observed with natural magnesian calcite (Figure, patterns 3 and 4). A shallow endothermic peak around 565 °C was also seen in both these cases.

The present study thus indicates that the dissociation of magnesian calcites is a function of the nature and extent of impurity in the lattice, and that presence of dolomite in a physical mixture with calcite does not affect the dissociation trend of calcite. A systematic differential thermal study with magnesian calcites of differing composition would be of considerable importance of estimation of the extent of Mg^{++} present in solid-solution in natural magnesian calcites. In such studies, however, the grain size and other affecting parameters need to be properly controlled.

Zusammenfassung. Es wurde die Dissoziationstemperatur für verschiedene synthetische und natürliche Calcite und Mg-Calcite bestimmt. Die Dissoziationstemperatur ist abhängig vom Mg-Gehalt des Gitters.

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Cocsulin: a New Bisbenzylisoquinoline Alkaloid from *Cocculus pendulus* Diels[1]

Confirmation of anticancer and hypotensive activity in the alkaloid fraction from leaves and stem of *Cocculus pendulus* Diels[2] has led to further chemical investigations and the isolation of pendulin, a new biscoclaurine base[3]. We now report a second new base, provisionally designated as cocsulin, from this fraction.

Cocsulin, $C_{35}H_{34}N_2O_5$[4] (M^+, 562), mp 272–274 °, $[\alpha]_D$ + 280 °, formed a picrate mp 194–196 °. Its IR-spectrum with maxima at 2907, 1621, 1575, 1504, 1453, 1372, 1269, 1198, 1119, 831 and 778 cm^{-1} indicated the presence of hydroxyl and ether functions and its substituted aromatic nature. The UV-spectrum of cocsulin was typical of a bisbenzylisoquinoline; a maximum at 284 nm shifting bathochromically to 304 nm on addition of alkali[5]. With H_2SO_4-HNO_3, cocsulin gave a blue coloration characteristic of bisbenzylisoquinoline alkaloids having a diphenylene dioxide function[6].

The NMR-spectrum of cocsulin integrated for 34 protons: 2 NMe singlets at τ 7.44 and 7.62, 1 OMe singlet at τ 6.15, 4 benzylic, 8-ring methylene and 2-ring methylene protons at τ 6.75, 7.29 and 5.98 respectively, and 10 aromatic protons (a shielded singlet at τ 3.86, a 2-proton singlet at τ 3.16 and a 7-proton multiplet between τ 2.40–3.39).

Treatment of methanolic solutions of cocsulin with diazomethane and diazoethane yielded *O*-methylcocsulin, $C_{36}H_{36}N_2O_5$ (M^+, 576) mp 212–214 °, $[\alpha]_D$ + 289 °, and *O*-ethylcocsulin, $C_{37}H_{38}N_2O_5$ (M^+, 590) mp 214–216 °, $[\alpha]_D$ + 225 °, respectively. The IR-spectrum of these compounds showed the absence of free hydroxyl functions and their NMR-spectra were similar to that of cocsulin except for an additional OMe singlet at τ 6.0 in the spectrum of *O*-methylcocsulin and an *O*-ethyl triplet at τ 8.48 and quartet at τ 5.74 (J, 11 Hz) in the spectrum of *O*-ethylcocsulin.

Comparison of *O*-methylcocsulin with an authentic sample of isotrilobine[7] established their identity. Cocsulin, isomeric with trilobine was, therefore, an *O*-demethylated derivative of isotrilobine, a *bis*benzylisoquinoline isolated from *Cocculus trilobus, Cocculus sarmentosus*[7] and *Stephania hernandiflora*[8]. In confirmation, cocsulin yielded a dimethiodide, $C_{38}H_{42}IN_2O_5$, identical in all respects to isotrilobine dimethiodide[9] and Hofmann degradation of this compound yielded a methine, $C_{38}H_{40}N_2O_5$, mp 114–117 °, that appeared identical with the reported isotrilobine methylmethine[10].

The location of the hydroxyl group of cocsulin followed from a consideration of the mass spectra of cocsulin and *O*-methylcocsulin. The M^+ peak in both spectra were prominent. The most important diagnostic peaks in the spectra of the trilobine type of alkaloids are those due to a doubly-charged ion m/e 175 (I) and a prominent ion m/e 350 (II)[11]. Both these peaks are present in the

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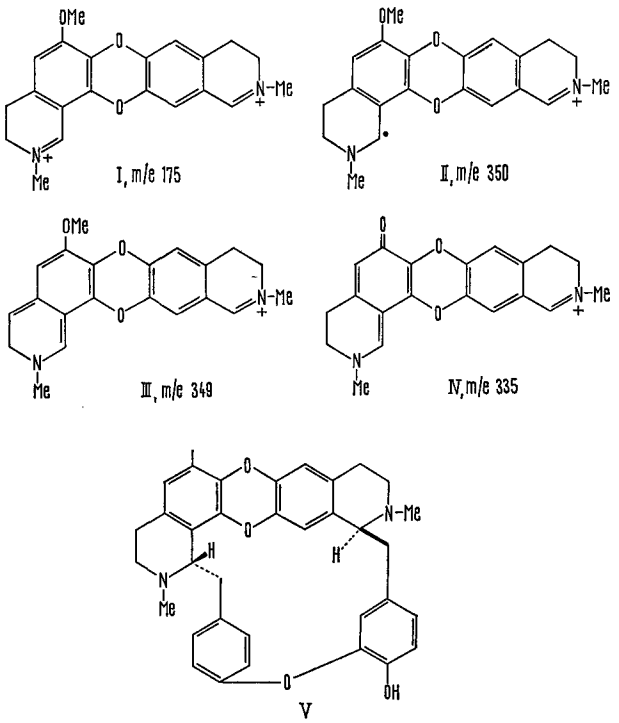

spectra of cocsulin and *O*-methylcocsulin as are also the abundant ions m/e 349 (III) and m/e 335 (IV) formed from II by the loss of a hydrogen atom and a methyl radical respectively. The presence of ions I, II, III and IV in the spectra of cocsulin and *O*-methylcocsulin is good evidence that the OMe group in cocsulin is attached to the tetrahydroisoquinoline portion and the hydroxyl to the benzylic half. Cocsulin can, therefore, be represented by the structure V with stereochemistry, since the stereochemistry of both centres in isotrilobine have been shown to have the S-configuration by examination of the fragments of Na/liq. NH_3 fisson[12].

Zusammenfassung. Ein neues *bis*benzylisochinolines Alkaloid vom Typ des Trilobins wird Cocsulin genannt, ($C_{35}H_{34}N_2O_5$), Schmp. 272–274°, $[\alpha]_D + 280°$, und ist aus Blättern und Stamm von *Cocculus pendulus* Diels isoliert und als Struktur V angegeben worden.

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Central Drug Research Institute, Lucknow (India), 29 September 1969.

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Bromal, the Product of Reaction of Aspartic Acid with N-Bromosuccinimide

The oxidative decarboxylation of α-amino acids by N-bromosuccinimide (NBS) has been studied by several workers[1]. Reported products of this reaction are CO_2, N_2 and the aldehyde or nitrile corresponding to the decarboxylated amino acid[1]. NBS has also been used to specifically degrade N-acylated tyrosyl peptides by selective cleavage of the tyrosyl carboxyl-peptide bond[2] giving smaller peptides or free amino acids. When aspartic acid was treated with NBS, in the only investigation reported of this reaction, 2 moles of CO_2 (and no N_2) were evolved by KÖNIGSBERG et al.[1]; no attempt was made to characterize the decarboxylation product. Aspartic acid is oxidized at pH 9.4 by hypobromite to cyanoacetic acid and dibromoacetamide[3].

When solvent extracts of reaction mixtures of NBS and aspartic acid were bioautographed against *Staphylococcus aureus* or *Candida albicans*, we observed large bioactive zones. The antimicrobial agent was prepared by treating aspartic acid (2 g) in pH 3.0 citric acid-K_2HPO_4 buffer (88 ml) with NBS (2.72 g) at room temperature for 15 min. Extraction with organic solvents gave a substance which had a single NMR-peak at δ 8.52 in CCl_4. The IR-spectrum in this solvent had peaks at 3.54 and 5.71 μ, suggesting an aldehyde, and other peaks at 7.39, 9.94, and 10.17 μ. The material formed an unstable 2,4-dinitrophenylhydrazone that decomposed when refluxed with methanol, giving the 2,4-dinitrophenylhydrazone of methyl glyoxylate, mp 148.0–149.0[4]. This material was identified by its NMR-spectrum: ($CDCl_3$) δ 3.97 (s, 3), 7.12 (s, 1), 8.0–8.6 (m, 2), 9.17 (d, 1), 14.38 (broad, 1) and elemental analysis. The formation of this derivative and the spectra of the precursor suggested that the antimicrobial substance was bromal[5]. This was confirmed by comparison of the NMR- and IR-spectra with those of authentic bromal (Aldrich).

The approximate time-course of the reaction was studied under our reaction conditions by determining the diameter of the zone of inhibition around bioautographed discs dipped in BuOH extracts of replicate reaction mix-

Anti-bacterial activity of bromal

Organism tested	Squibb culture No.	M.I.C. μg/ml
Staphylococcus aureus 209p	1276	23.9
Escherichia coli	2975	47.8
Proteus vulgaris	8504	20.5
Pseudomonas aeruginosa	3840	9.0
Salmonella schottmuelleri	3850	47.8
Mycobacterium tuberculosis, BCG	5516	4.5
Candida albicans	5314	95.6
Trichophyton mentagrophytes	2637	383

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