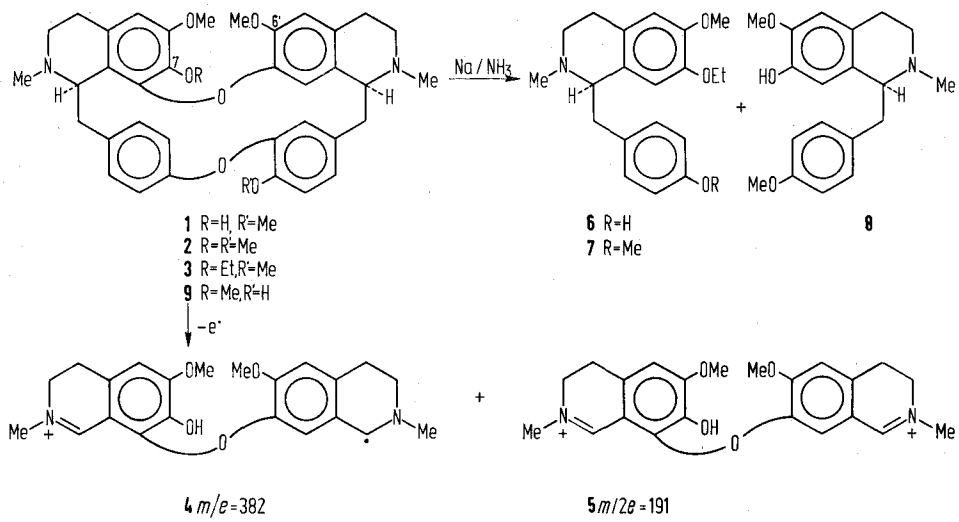
Antibiotics from Higher Plants. *Thalictrum rugosum*. Thalrugosamine, a New *Bis*benzylisoquinoline Alkaloid Active vs *Mycobacterium smegmatis*

Recently the isolation and structure determination of thalrugosine and thalrugosidine, new *bis*benzylisoquinoline alkaloids active in vitro vs. *M. smegmatis* was reported from extracts of *Thalictrum rugosum* Ait. (*T. glaucum* Desf.)[1]. At the same time, the previously known *bis*-benzylisoquinoline bases obamegine and thalidasine were shown to be active and present in these extracts. Subsequently, a minor base has been isolated from the mother-liquors of the thalrugosine crystallization and is slightly active in vitro against *M. smegmatis* ATCC 607. This new base is named Thalrugosamine and its structure has been determined to be **1**. Thalrugosamine; m.p. 122–5°; $C_{37}H_{40}N_2O_6$ (M^+ 608); analyzes correctly (C, H, N); $[\alpha]_D^{30}$ + 280 (MeOH); λ_{max} (MeOH) 282 nm (log ε 3.91); nmr δ ($CDCl_3$) 2.51 and 2.55 (s, 2×NMe), 3.60, 3.78 and 3.88 (s, 3×OMe), 6.3–7.5 (m, 10×ArH); c.d. $[\Theta]_{293}$ + 912, $[\Theta]_{280}$ + 700, $[\Theta]_{274}$ + 610, $[\Theta]_{225}$ + 16500, $[\Theta]_{220}$ + 14000; mass spectrum, M^+ = 608 (51%), 382 (23%) (**4**), 381 (74%), 367 (29%), 206 (93%), 205 (28%), 192 (80%), 191 (100%) (**5**), 190 (39%), 176 (23%), 175 (28%), 174 (39%), 168 (28%), 149 (90%), etc; and was converted smoothly to its methyl ether (**2**) with etheral diazomethane. The product gave identical *ir-*, *uv-*, *tlc* and *nmr*-spectra (including peaks at 2.55, 2.64 (2×NMe) and 3.20, 3.61, 3.79 and 3.90 δ (4×OMe) with *O*-methyloxyacanthine (**2**) prepared with diazomethane from authentic oxyacanthine (**9**). The new *O*-Me resonance at 3.20 δ is characteristic of the highly shielded C_7 position in this ring system when the base pairs are of opposite absolute configuration[2]. Placement of the phenolic OH group in the upper portion of the molecule is also supported by the appearance of important fragments **4** and **5** in the mass spectrum of **1**[3]. The absolute configuration depicted follows from correspondence of cd curves of **1** and **2** derived both from **1** and **9**. In confirmation, thalrugosamine ethyl ether (**3**) (pmr 0.65 δ (t, OCH_2CH_3) and 3.34 δ (q, OCH_2CH_3)) was cleaved with sodium in liquid ammonia to give **6** in which the free OH of **1** was marked by the Et group. Treatment of **6** with diazomethane gave **7** which was identical (including cd spectrum) with a sample prepared similarly from thalrugosine ethyl ether. The second cleavage fragment (**8**) was identical (including cd spectrum) to the corresponding fragment prepared from *O*-methyloxyacanthine (**2**). The structure and absolute configuration of thalrugosamine is, therefore, **1**.

Thalrugosamine represents the 3rd ring system of bisbenzylisoquinoline alkaloid lacking in methylation at C_7 which has been isolated from antibacterially active extracts of *Thalictrum rugosum* and is the 5th member of this well known class of alkaloids[4] to show reproducible, though weak, activity in vitro against mycobacteria[5].



Zusammenfassung. Charakterisierung und Strukturaufklärung eines neuen Alkaloides, Thalrugosamin aus *Thalictrum rugosum*.

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1 L. A. MITSCHER, WU-NAN WU, R. W. DOSKOTCH and J. L. BEAL, Chem. Commun. *1971*, 589.

2 I. R. C. BICK, J. HARLEY-MASON, N. SHEPPARD and M. J. VERNEGO, J. chem. Soc. (C) *1961*, 1896.

3 D. C. DEJONGH, S. R. SHRADER and M. P. CAVA, J. Am. chem. Soc. *88*, 1052 (1966).

4 T. KAMETANI, *The Chemistry of the Isoquinoline Alkaloids* (Elsevier Publishing Co., New York, N. Y. 1969).

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