A Biomimetic Synthesis of Agelasidine A

Yoshiyasu Ichikawa,* Tikako Kashiwagi, and Noriko Urano

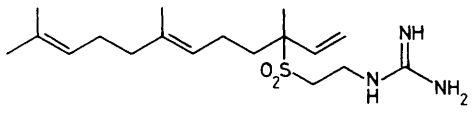
Faculty of Education, Mie University, 1515 Kamihama, Tsu 514, Japan

Agelasidine A was synthesised based on the strategy modelled on the hypothesis of biosynthesis; this strategy provided an efficient three-step synthesis of agelasidine A from farnesol.

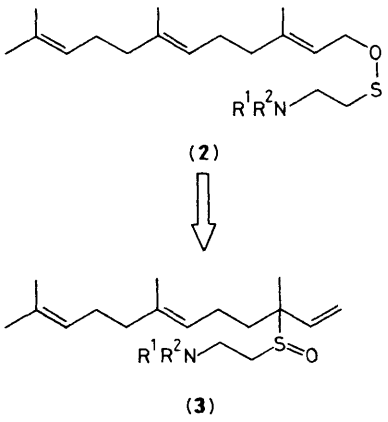
Agelasidine A (**1**) is a sesquiterpene with a unique structure characterised by a quaternary carbon atom attached to a sulphur atom.[1]

The biosynthesis of (**1**) was postulated to be derived from farnesol through sigmatropic rearrangement of its aminoethyl sulphenic acid ester (**2**) as shown in Scheme 1.[2] [2,3] Sigmatropic rearrangement followed by oxidation of the sulphoxide (**3**) to sulphone and introduction of guanidine moiety would be a probable biosynthetic pathway of this molecule.

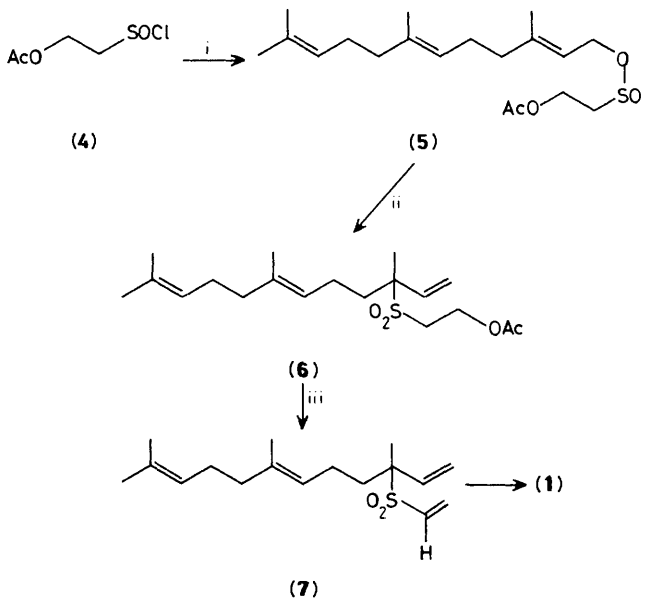
Based on this biogenetic line, a new synthetic strategy was developed as shown in Scheme 2. The crucial step of this route was the [2,3]sigmatropic rearrangement of allylic sulphinate to



(**1**)



Scheme 1



Scheme 2. *Reagents and conditions*: i, farnesol, pyridine; ii, 140 °C, DMF; iii, guanidine.

allylic sulphone.[3] 2-Acetoxy ethyl sulphinic acid chloride (**4**) was chosen as synthetic equivalent of amino ethyl sulphenic acid, and prepared from the corresponding thiol acetate with sulphuryl chloride.[4] Treatment of farnesol with (**4**) in pyridine gave the sulphinic acid ester (**5**) in 97% yield. Rearrangement of allylic sulphinate (**5**) to allylic sulphone was carried out by heating a solution of (**5**) in dimethylformamide (DMF) at 140 °C for 35 min[5] to provide the allylic sulphone (**6**) in 78% yield {^{1}H n.m.r. (200 MHz, $CDCl_3$) data for (**6**): δ 1.51 (3H, s), 1.57 (3H, s), 1.60 (3H, s), 1.68 (3H, s), 1.9—2.1 (8H), 2.02 (3H, s), 3.26 (2H, t, *J* 6 Hz), 4.51 (2H, t, *J* 6 Hz), 5.0—5.15 (2H), 5.40 (1H, d, *J* 18 Hz), 5.52 (1H, d, *J* 11 Hz), 6.05 (1H, dd, *J* 18, 11 Hz)}. Reaction of this β-acetoxy sulphone (**6**) with large excess of guanidine gave the vinyl sulphone (**7**) which successively received the addition of guanidine to furnish agelasidine A (**1**) in 66% yield.

This strategy presented a remarkably simple laboratory synthesis of (**1**) in 3 steps from farnesol (compared with the previous synthesis which involved 8 steps),[6] and furnished a valuable support of the proposed biosynthesis of this molecule.

I would like to express my deep appreciation and gratitude to Profs. M. Isobe and T. Goto at Nagoya University for their helpful discussions and experimental support. Financial support from the Agricultural Chemical Research Foundation is gratefully acknowledged.

Received, 7th February 1989; Com. 9/00591I

References

1 H. Nakamura, H. Wu, J. Kobayashi, Y. Ohizumi, Y. Hirata, T. Higashijima, and T. Miyazawa, *Tetrahedron Lett.*, 1983, **24**, 4105; R. J. Capon and D. J. Faulkner, *J. Am. Chem. Soc.*, 1984, **106**, 1819.
2 H. Nakamura, H. Wu, J. Kobayashi, M. Ohizumi, and Y. Hirata, *J. Org. Chem.*, 1985, **50**, 2494.
3 A. C. Cope, D. E. Morrison, L. Field, *J. Am. Chem. Soc.*, 1950, **72**, 59.
4 S. Thea and G. Cevasxo, *Tetrahedron Lett.*, 1987, **43**, 5193.
5 K. Hiroi, R. Kitayama, and S. Sato, *J. Chem. Soc., Chem. Commun.*, 1983, 1473.
6 Y. Ichikawa, *Tetrahedron Lett.*, 1988, **29**, 4957.