Tetrahedron Letters No. 39, pp 3503 - 3506, 1974. Pergamon Press. Printed in Great Britain.

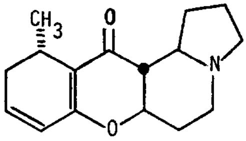
A MODEL FOR THE SYNTHESIS OF THE DIENONE ELAEOCARPUS ALKALOIDS[1]

Tappey H. Jones and Paul J. Kropp*[2]

Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514

(Received in USA 25 July 1974; received in UK for publication 16 August 1974)

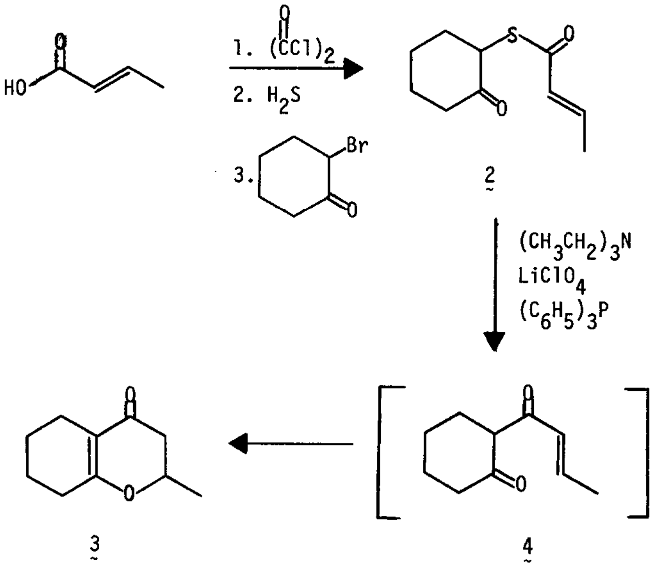
The dienone alkaloids isomeric with elaeocarpiline (1) comprise the most numerous and widely distributed indolizidine alkaloids found in the rain-forest trees of the genus Elaeocarpus.[3] Although the A-ring aromatic indolizidine Elaeocarpus alkaloids have been successfully synthesized,[3] the routes described are not applicable to elaeocarpiline and its isomers because of their labile cyclohexadiene moiety.



1

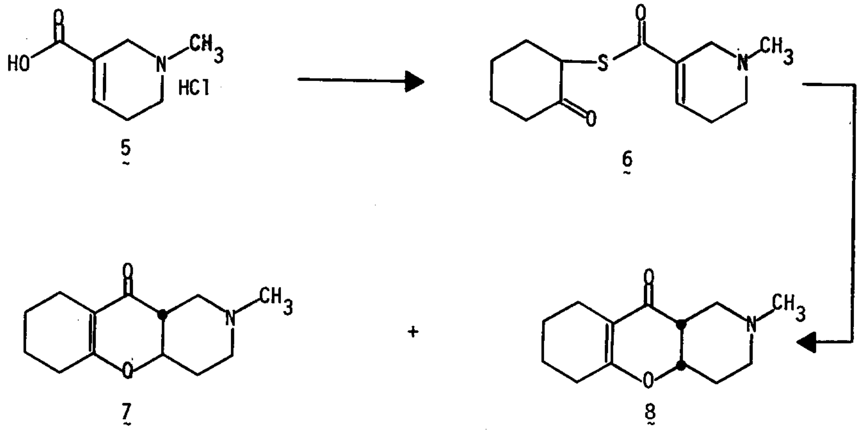
We wish to report here a model synthesis for the dienone Elaeocarpus alkaloids which is convergent about the dihydro-γ-pyrone ring of these compounds. This model is based on a modification of the β-diketone synthesis developed by Eschenmoser,[4] since γ,δ-unsaturated β-diketones (e.g., 4) are known to undergo facile cyclization to dihydro-γ-pyrones.[5]

Initial experiments starting with crotonic acid showed that the modified Eschenmoser sequence can lead to the regiospecific formation of non-functionalized dihydro-γ-pyrones. Crotonic acid was treated in succession with oxalyl chloride, hydrogen sulfide in pyridine,[6] and α-bromocyclohexanone[7] in triethylamine and methylene chloride to give α-thiolcrotonylcyclohexanone (2) in 31% isolated yield: bp 160° (0.2 mm); mp 47°; ν_{max} 1715, 1670, and 1635 cm^{-1}; nmr τ 2.90 (d of q, J = 6.6 and 15.3, 1, CH_3-C$\underline{H}$=) and 8.06 (d of d, J = 6.5 and 1.5, 3, $-CH_3$); m/e 198.0711.



A benzene solution of the keto thiolester 2 was then treated with triethylamine, anhydrous lithium perchlorate, and triphenylphosphine to give 2-methyl-5,6,7,8-tetrahydrochromanone (3) in 33% isolated yield; bp 100-114° (0.6 mm); DNPH, mp 196°; ν_{max} 1665 and 1620 cm^{-1}; nmr τ 8.57 (d, J = 6.4, -CH_3); lit.[8] bp 137° (18 mm); DNPH mp 196°; lit.[9] nmr τ 8.6 (d, J = 6.6, -CH_3).

Substitution of arecaidine hydrochloride (5)[10] for crotonic acid in this sequence allowed the inclusion of a teritary amine function and provided a model closely corresponding to the dienone *Elaeocarpus* alkaloids. A methylene chloride solution of 5 was treated with oxalyl chloride, the solvent removed under vacuum, and the residue treated with hydrogen sulfide in pyridine.[6] After removal of the solvent under reduced pressure, the residue was taken up in dimethyl sulfoxide and treated with triethylamine and α-bromocyclohexanone for 90 hr to give α-thiolarecaidinylcyclohexanone (6) as the only high molecular weight product: ν_{max} 2850, 2792, 1720, 1660, and 1626 cm^{-1}; *m/e* 253.1141. A methylene chloride solution of 6 was then treated with triethylamine, anhydrous lithium perchlorate, and triphenylphosphine for 48 hr to give *N*-methyl-2-aza-1,2,3,4,4a,5,6,7,8,9a-decahydroxanth-9-one as two isomers (7 and 8) separable by vpc. The *trans* isomer 7 was a solid: mp 102-105°; ν_{max} 2852, 2790, 1665, and 1616 cm^{-1}; The coupling pattern for the 4a proton at τ 6.0 was identical with that shown for the correspond-



ing proton of the trans-fused dienone Elaeocarpus alkaloids.[11] The cis isomer was a liquid: ν_{max} 2850, 2797, 1667, and 1618 cm^{-1}; The mass spectra of both isomers were identical: m/e 221.1413, 97 (80) and 96 (100). This fragmentation pattern corresponds to that reported for the dienone Elaeocarpus alkaloids.[11]

Application of this approach to the synthesis of the dienone Elaeocarpus alkaloids is planned.

Acknowledgements. The authors are indebted to Donna M. Frieze for preparative work leading to arecaidine hydrochloride, and the Merck Company Foundation for financial support.

REFERENCES AND FOOTNOTES

1. Taken from the Ph.D. dissertation of Tappey H. Jones, University of North Carolina, 1974.
2. Alfred P. Sloan Research Fellow.
3. S. R. Johns and J. A. Lamberton in "The Alkaloids," Vol. XIV, Academic Press, Inc., London, 1973, Chapter 8.
4. M. Roth, P. Dubs, E. Gotschi, and A. Eschenmoser, Helv. Chim. Acta, **54**, 710 (1971).
5. W. Dieckmann, Chem. Ber., **53**, 1772 (1920).

6. A. Fredga and H. Bauer, *Arkiv Kemi*., **2**, 115 (1950).

7. J. Allinger and N. L. Allinger, *Tetrahedron*, **2**, 64 (1958).

8. S. Gelin, R. Gelin, and G. Champetier, *C*. *R*. *Acad*. *Sci*., *Paris*, *Ser*. *C*, **263**, 1029 (1966).

9. R. Gelin, S. Gelin, and R. Dolmazon, *Tetrahedron Lett*., 3657 (1970).

10. T. F. Daukova, E. A. Sidorova, and N. A. Preobrazhenskii, *Zhur*. *Obshchei Khim*., **11**, 934 (1941); *Chem*. *Abstr*., **37**, 381 (1943).

11. S. R. Johns, J. A. Lamberton, and A. A. Sioumis, *J*. *Aust*. *Chem*., **22**, 793 (1969).