Tetrahedron Letters No. 46, pp 4553 - 4556, 1973. Pergamon Press. Printed in Great Britain.

THE CHEMISTRY OF PROHOMOERYTHRINADIENONE I.

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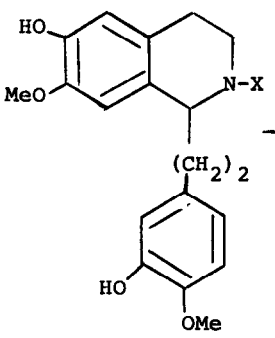
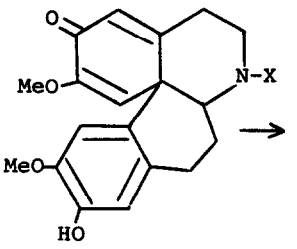
(Received in USA 13 August 1973; received in UK for publication 4 October 1973)

The homoerythrina alkaloids from Cephalotaxus[1] and Schellhammera[2] are proposed to originate from a 1-phenethyltetrahydroisoquinoline I, through in vivo phenolic coupling to the prohomoerythrinadienone II and according to a sequence of transformations analogous to the biosynthesis of the Erythrina alkaloids.[3] To date, this biogenetic proposal has not been completely[4] demonstrated in the laboratory. An earlier attempt by Kametani[5] to prepare the prohomoerythrinadienone II from the N-methylphenethyltetrahydroisoquinoline I (X = Me) failed to yield the dienone II, but instead gave a myriad of products derived from II. During the course of a biogenetic-type synthesis of some homoerythrina alkaloids, we have subjected the trifluoroacetamide of I to various oxidative coupling reactions. We wish to report at this time the first synthesis of the key prohomoerythrinadienone II (X = $COCF_3$) and its facile rearrangement to the homoaporphine skeleton III. This latter transformation constitutes the first synthesis of a homoaporphine alkaloid via a dienone-phenol rearrangement.



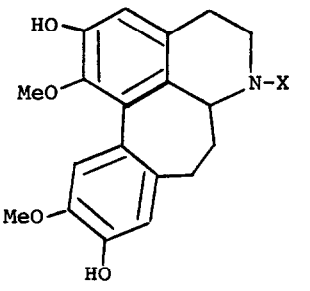
I



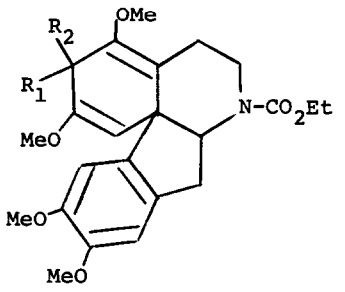
II

HOMOERYTHRINA ALKALOIDS

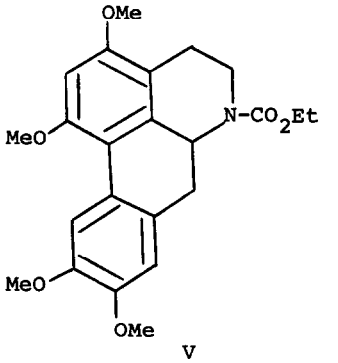
II $\xrightarrow[CH_2Cl_2]{BF_3\text{-}Et_2O}$



III



IV



V

The phenethyltetrahydroisoquinoline I [$C_{21}H_{22}F_3NO_5$, X = $COCF_3$, m.p. 129-130°C][8] was prepared by the procedure of Teitel and Brossi[6] and subsequent acetylation with trifluoroacetic anhydride in pyridine. When I (X = $COCF_3$) was oxidized with $VOCl_3$[7] (2.5 equiv.) in methylene chloride, the expected dienone II [$C_{21}H_{20}F_3NO_5$] was isolated by crystallization in a yield of 35%[9] [m.p. 198.5-200°; i.r. ($CHCl_3$) 1684 cm^{-1}, 1667 cm^{-1}, 1644 cm^{-1}, 1612 cm^{-1}; λ_{max}^{MeOH} 242(log ε 4.33), 284(log ε 3.87)]. Addition of excess boron trifluoride etherate to a methylene chloride solution of the dienone trifluoroacetamide II resulted in a brilliant red solution which decolorized after stirring for several hours at room temperature. Following an aqueous work-up and preparative layer chromatography, the homoaporphine III was isolated in 75% yield [$C_{21}H_{20}F_3NO_5$, m.p. 237.5-239°; i.r. ($CHCl_3$) 3531 cm^{-1}, 1686 cm^{-1}; λ_{max}^{MeOH} 210(log ε 4.61), 267(log ε 4.06), 287(log ε 4.00)].

Battersby[10] has shown that several naturally occurring homoaporphines from Kreysigia multiflora are derived via direct phenolic coupling of a phenethyltetrahydroisoquinoline precursor. Our synthesis of a homoaporphine via a dienone-phenol rearrangement should open new possibilities for the biogenesis of certain naturally occurring homoaporphine alkaloids. It is also significant that the analogous proerythrinadienone system IV (R_1R_2 = O) has never been successfully rearranged to an aporphine skelton.[11] Kametani[12] only recently succeeded in effecting a rearrangement of dienol IV (R_1 = H, R_2 = OH) to an aporphine V in less than 1% yield with methyl fluorosulfonate. Undoubtedly the additional methylene group of the prohomoerythrinadienone allows for a more propitious transition state for the dienone-phenol rearrangment. We shall report shortly on other transformations of the prohomoerythrinadienone II and its conversion to homoerythrina alkaloids.

Acknowledgement: The initial phase of this work was supported in part by Institutitional Research Grant No. IN-40K to The University of Michigan from the American Chemical Society.

References

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