THE CHEMISTRY OF PROHOMOERYTHRINADIENONE I.

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The homoerythrina alkaloids from Cephalotaxus¹ and Schellhammera² 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 completely⁴ demonstrated in the laboratory. An earlier attempt by Kametani⁵ 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 = COCF₃) 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.
\begin{align*}
\text{I} & \xrightarrow{\text{BF}_3-\text{Et}_2\text{O}, \text{CH}_2\text{Cl}_2} \text{II} \\
\text{II} & \rightarrow \text{III} \\
\text{III} & \rightarrow \text{IV, V} \\
\end{align*}
The phenethyltetrahydroisoquinoline I \([C_{21}H_{22}F_3N_O5, X = COCF_3, \text{m.p. } 129-130^\circ C]\) 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 \(\text{VOCl}_3\) \(^7\) (2.5 equiv.) in methylene chloride, the expected dienone II \([C_{21}H_{20}F_3N_O5]\) was isolated by crystallization in a yield of 35\% \(^9\) [m.p. 198.5-200\(^\circ\)]; i.r. \((\text{CHCl}_3) 1686 \text{ cm}^{-1}, 1667 \text{ cm}^{-1}, 1644 \text{ cm}^{-1}, 1612 \text{ cm}^{-1}; \lambda_{\text{MeOH}}^{\text{max}} 242(\log \varepsilon 4.33), 284(\log \varepsilon 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_3N_O5, \text{m.p. } 237.5-239^\circ\]; i.r. \((\text{CHCl}_3) 3531 \text{ cm}^{-1}, 1686 \text{ cm}^{-1}; \lambda_{\text{MeOH}}^{\text{max}} 210(\log \varepsilon 4.61), 267(\log \varepsilon 4.06), 287(\log \varepsilon 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 \((R_1R_2 = 0)\) has never been successfully rearranged to an aporphine skeleton.\(^{11}\) 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 rearrangement. We shall report shortly on other transformations of the prohomoerythrinadienone II and its conversion to homoerythrina alkaloids.
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References

8. All new compounds gave satisfactory elemental analyses.
9. A 45% yield was actually obtained based on recovered starting material. Yields have not yet been maximized in this reaction.