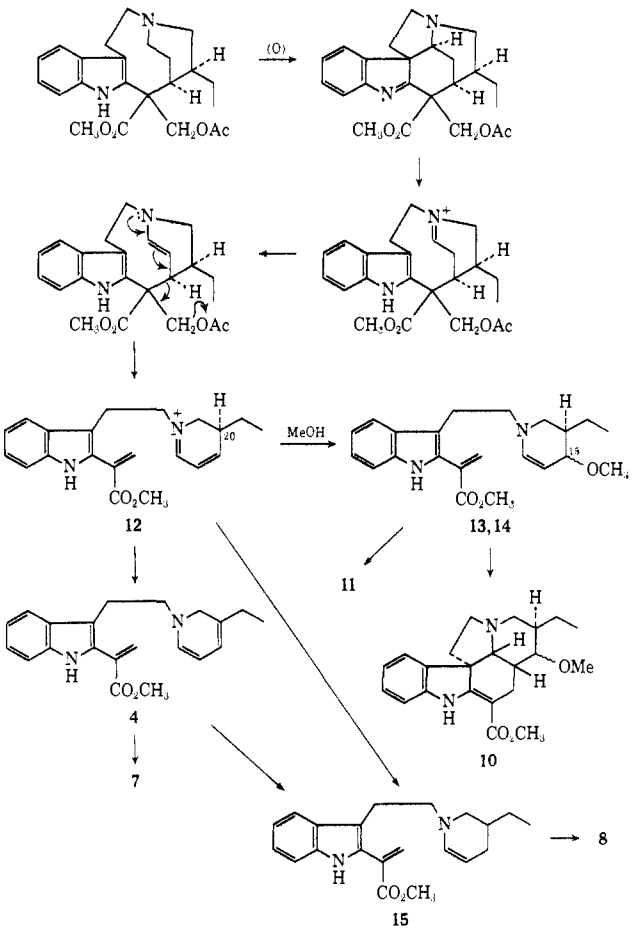
tion to pseudocatharanthine (**7**) and hydrogen transfer to **12**. The intermediate **15** from the latter reaction then cyclizes to dihydropseudocatharanthine (**8**).[15]

Scheme I



We would like to suggest that these experiments demonstrate not only the separation of an "*Iboga* synthetase" model from earlier, less specific reaction conditions but augur well for the synthesis of indole alkaloids based on the emerging chemistry of dihydropyridine acrylic esters, since in spite of the present low yields, transformations involving stereocontrol from one family to another are now possible.[16]

Acknowledgment. This work was supported by grants from the National Institutes of Health and the National Science Foundation.

(15) It is interesting to note that the (±)-dihydropseudocatharanthine (**8**) from this reaction is capable of formation in optically active form, but in conformity with earlier experience the product can easily racemize. The milder conditions (MeOH; 25–80°) used in the formation of **10** and **11**, however, allow considerable retention (70–80%) of optical purity.

(16) In this and the subsequent two communications all of the reaction products were identified by spectroscopic and tlc comparison with authentic samples of the natural alkaloids, with the exception of compounds **10** and **11** which were assigned these structures on the basis of mass spectral, uv, and ORD data.[5] Thus, **10** and **11** had λ_{max}^{MeOH} 226, 298, and 328 nm; *m/e* 368 (M^+, 40%), 337 ($M^+ - OCH_3$, 19%), and 154 (100%); **10** showed $(\Phi)_{345\ nm}$ +25,000 and **11** had $(\Phi)_{345\ nm}$ −28,000.

A. I. Scott,* C. C. Wei

Sterling Chemistry Laboratory, Yale University
New Haven, Connecticut 06520

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Regio- and Stereospecific Models for the Biosynthesis of the Indole Alkaloids. The *Corynanthe–Aspidosperma* Relationship

Sir:

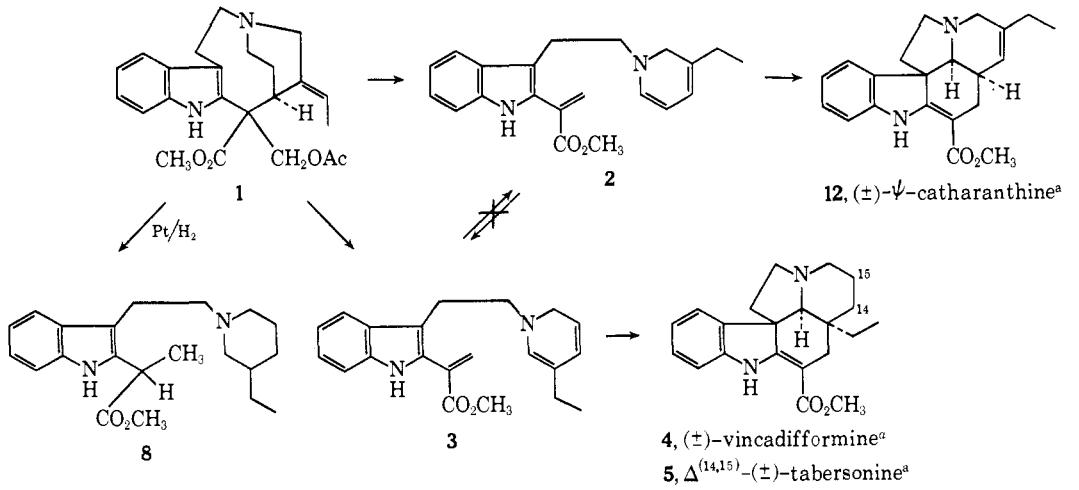
In the previous communication[1] we described the regio- and stereospecific conversion of stemmadenine acetate (**1**) to the *Iboga* alkaloids *via* dehydrosecodine A (**2**). In order to define the mechanism and conditions whereby a mixture of *Aspidosperma* and *Iboga* types were formed in acetic acid at high temperatures[2] we have developed a technique for the specific generation of the isomeric intermediate *chano* structure, dehydrosecodine B (**3**) in the expectation that the cyclization reaction of **3** would lead to a preponderance of the *Aspidosperma* type of alkaloid exemplified by vincadifformine (**4**) and tabersonine (**5**). The experimental design was guided by the reactions which have already been noted[2] in acetic acid at high temperature, *viz.* acetylation and disproportionative oxidation and reduction.[3] In the event, the reaction proceeded with complete regio- and stereospecific control (see Scheme I).

Thus the simple isomerization mechanism (Scheme II) suggested earlier for the conversion of stemmadenine to both *Iboga* and *Aspidosperma* alkaloids can be separated from the accompanying *redox* mechanism as follows. Stemmadenine *O*-acetate (**1**) (as the hydrochloride salt) was heated at 150° on a silica gel surface[1] for 25 min. Preparative tlc of the reaction mixture afforded some unchanged starting material together with a small but reproducible yield (0.15–0.2%) of (±)-vincadifformine (**4**) identical[4] with the natural, racemic alkaloid. No trace of tabersonine (**5**) could be detected in this reaction. We suggest that direct isomerization of **1** to the isostemmadenine acetate (**6**) takes place. This is followed by the reverse Mannich reaction shown in Scheme II which generates dehydrosecodine B (**3**). The latter in turn is reduced by hydride to secodine B (**7**) whereupon cyclization of this tetrahydropyridine acrylic ester completes the regio- and stereospecific production of (±)-vincadifformine from a *Corynanthe* alkaloid.

An alternative method of generating the dehydrosecodine B system embodies the observations that stemmadenine acetate (**1**) is quite sensitive to aerial oxidation in acetic acid solution and that catalytic reduction of **1** (Pt/H_2) gave a 75% yield of tetrahydrosecodine[4] (**8**). This type of reaction which proceeded without deliberate control in earlier experiments[2] can be sequentially studied by platinum-catalyzed oxidation of **1** regiospecifically to precondylocarpine acetate[5]

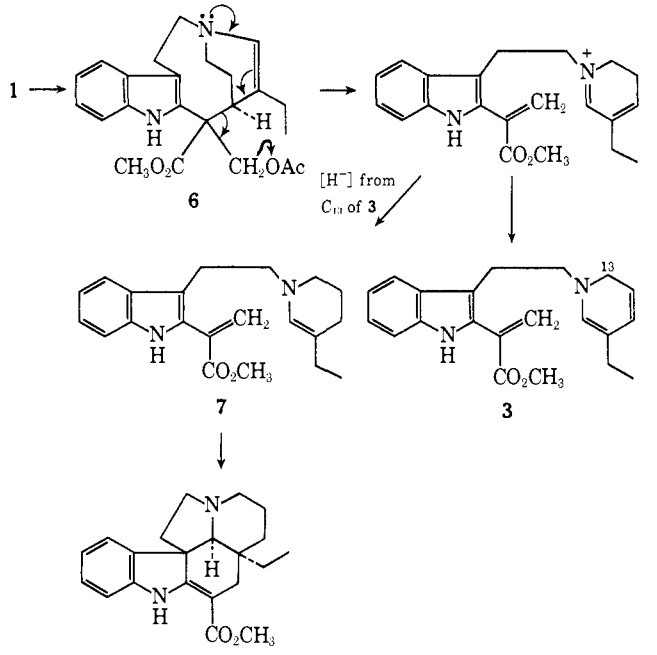
(1) A. I. Scott and C. C. Wei, *J. Amer. Chem. Soc.*, **94**, 8263 (1972).
(2) A. A. Qureshi and A. I. Scott, *Chem. Commun.*, 947 (1968).
(3) M. Gorman, N. Neuss, and N. J. Cone, *J. Amer. Chem. Soc.*, **87**, 93 (1965).
(4) (±)-Vincadifformine and (±)-tabersonine were identified by procedures referred to in ref 1, footnotes 11 and 16, and their racemic nature confirmed $[\alpha]_{300-600\ nm}$ 0°. Tetrahydrosecodine (**8**) was obtained as the racemic version $[\alpha]_{300-600\ nm}$ 0° with tlc and spectroscopic data identical with natural material (G. A. Cordell, G. F. Smith, and G. N. Smith, *Chem. Commun.*, 189 (1970)): mass spectrum *m/e* 342 (10%), 126 (100%); λ_{max}^{MeOH} 226, 278 (sh), 286, 292 nm; nmr δ($CDCl_3$) 0.9 (t, 3 H, CH_2CH_3), 1.55 (d, 3 H, CH_3CHCO_2Me), 3.64 (s, 3 H, $COOCH_3$), 4.1 (q, 1 H, $CH_3CHCO_2CH_3$), 7.0–7.5 (4 H, m, Ar H), 8.4 (s, 1 H, >NH).
(5) Precondylocarpine acetate: λ_{max}^{MeOH} 221, 273, 282 (sh), 291 (sh) nm; *m/e* 394 (50%), 335 (98%), 321 (100%), 278 (88%), 275 (90%); nmr δ ($CDCl_3$) 1.55 (d, 3 H, C=CHCH_3), 3.60 (s, 3 H, $COOCH_3$), 5.2 (q, 1 H, =$CH$$CH_3$), 6.8–7.2 (m, 4 H, Ar H).

Scheme I



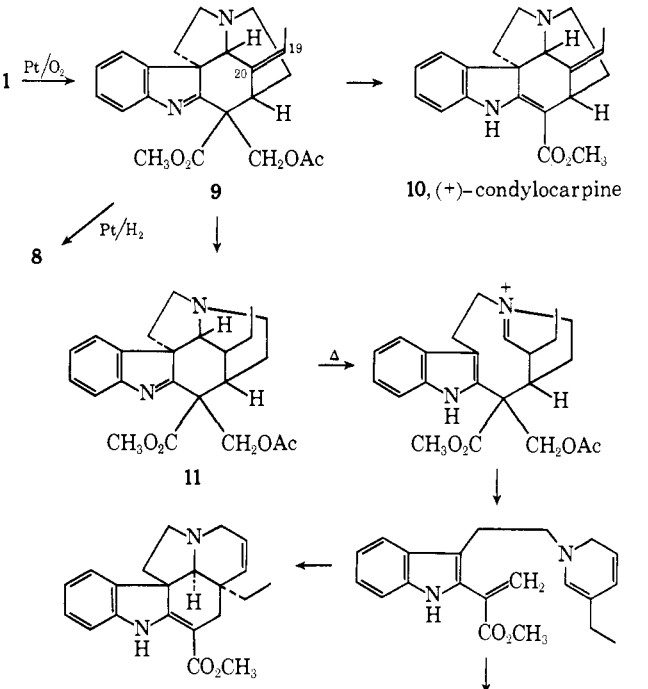
[a] The (−) form is illustrated.

Scheme II



[a] The (−) form is illustrated.

Scheme III



[a] The (−) form is illustrated.

(**9**), the structure of which was determined spectroscopically (mass, uv, nmr spectra) and confirmed by the conversion of **9** to (+)-condylocarpine (**10**) in refluxing methanolic sodium methoxide.[6] Reduction of the 19,20 double bond of **9** afforded dihydroprecondylocarpine acetate (**11**) (*m/e* 396) together with tetrahydrosecodine (**8**).

When subjected to thermolysis (150°, silica gel, 25 min), **11** yielded a separable mixture of (±)-tabersonine[4] (**5**) (0.2%) and (±)-vincadifformine[4] (**4**) (0.2%). No trace of the *Iboga* compound pseudocatharanthine (**12**) could be detected. From this experiment we conclude that the reaction proceeds by generation of dehydrosecodine B (**3**) without isomerization to the A isomer **2** according to Scheme III. These processes reveal the hidden complexities of our earlier overall reaction scheme[7] and although no attempt has yet been made to optimize the yields of the separated "*Aspidosperma* synthetase" model, it is interesting to note that together with the reactions of the A series, this sequence illustrates a working facsimile for the known conversion of stemmadenine to catharanthine and tabersonine in *Vinca rosea* with an efficiency comparable to the natural process and opens the general question of the specificity of the enzymes of indole alkaloid-producing plant systems.

Acknowledgment. This work was supported by grants from the National Institutes of Health and the National Science Foundation.

(6) *Cf.* A. Walser and C. Djerassi, *Helv. Chim. Acta*, **48**, 391 (1965) for an analogous experiment with precondylocarpine. We thank Professor Djerassi for a valuable gift of the latter alkaloid.

(7) A. A. Qureshi and A. I. Scott, *Chem. Commun.*, 948 (1968).

A. I. Scott,* C. C. Wei
Sterling Chemistry Laboratory, Yale University
New Haven, Connecticut 06520
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