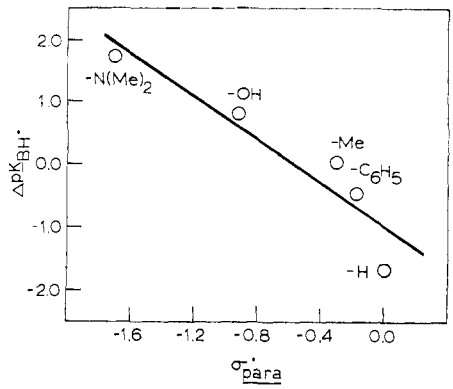
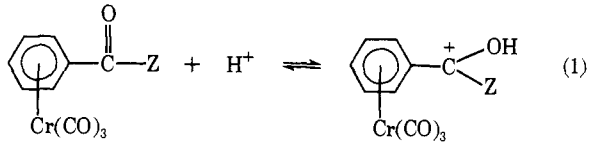


Figure 1. Plot of the differences between the pK_{BH^+} values for the free and complexed benzoyl compounds *vs.* σ^+_p of the α substituent of the benzoyl compound.

protonation to give the corresponding α-hydroxybenzyl cations.



(1)

The basicities of substituted benzaldehydes,[8] acetophenones,[9] benzoic acids,[10] benzamides,[7] and benzophenones[11] have been quantitatively evaluated by determining the pK_{BH^+} ($-\log K$) for the reverse of eq 1 for the conjugate acids of these compounds using spectrophotometric methods and tabulated Hammett acidity function values of aqueous sulfuric acid mixtures.

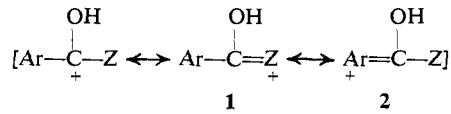
The pK_{BH^+} values for the free and complexed benzoyl compounds which we have determined are presented in Table I. From the ΔpK_{BH^+} values, which are the differences between the pK_{BH^+} values for the free and complexed compounds, it is seen that tricarbonylchromium moiety increases the stability of the conjugate acids of benzaldehyde and benzophenone, has little effect on that of acetophenone, and actually decreases the stability of the conjugate acids of benzoic acid and N,N-dimethylbenzamide.

Table I. Basicity of Free and Tricarbonylchromium-Complexed Benzoyl Compounds

Compd	pK_{BH^+} for free compd[a]	pK_{BH^+} for complex[b]	ΔpK_{BH^+}[c]
C_6H_5CHO	−7.11 (−7.10)[d]	−5.46	−1.65
$C_6H_5COC_6H_5$	−6.13 (−6.18)[e]	−5.68	−0.45
$C_6H_5COCH_3$	−5.91 (−6.15)[f]	−5.96	0.05
C_6H_5COOH	−7.20 (−7.26)[g]	−8.02	0.82
$C_6H_5CON(CH_3)_2$	−1.37 (−1.62)[h]	−3.10	1.73

[a] Maximum error estimated to be ±0.30 pK unit. [b] Maximum error estimated to be ±0.50 pK unit. [c] The difference between the free and complexed pK_{BH^+} values. [d] Reference 8. [e] Reference 11 [f] Reference 9. [g] Reference 10. [h] Reference 7.

From Figure 1 it is seen that a fair correlation exists between ΔpK_{BH^+} and the σ^+_p for the carbonyl substituent (slope = −1.72 ± 0.38). A correlation that is



almost as good is obtained with σ_p (slope = −3.39 ± 0.88), but a very poor correlation with σ_m was obtained. This suggests that, as resonance structure **1** becomes more important in stabilizing the conjugate acid of the benzoyl compound, resonance structure **2**[12] becomes less important. Thus the electron-withdrawing inductive effect of the tricarbonylchromium[4] becomes more important than the electron-donating ability of the tricarbonylchromium as resonance structure **2** becomes less important. In other words, as the need for stabilization of the benzylic cation by the aromatic system becomes less, the tricarbonylchromium moiety participates less in its stabilization and the ever present electron-withdrawing characteristic of the tricarbonylchromium becomes evident.

The thermodynamic stabilities of the free and complexed benzyl cations and tropylium ion also substantiate the variable cation-stabilizing ability of the tricarbonylchromium group. The complexed benzyl cation is >5.5 pK units more stable than the free cation, but complexed tropylium ion is only 1.6 pK units more stable than the free tropylium ion, which is, of course, much more stable than the free benzyl cation.[1a]

(12) Resonance structure **2** is meant to show delocalization of the positive charge by the free aryl or complexed aryl group and is not meant to imply a mechanism of delocalization of the positive charge by the (aryl)tricarbonylchromium group.

(13) American Chemical Society Petroleum Research Fund Graduate Fellow, 1968–1969.

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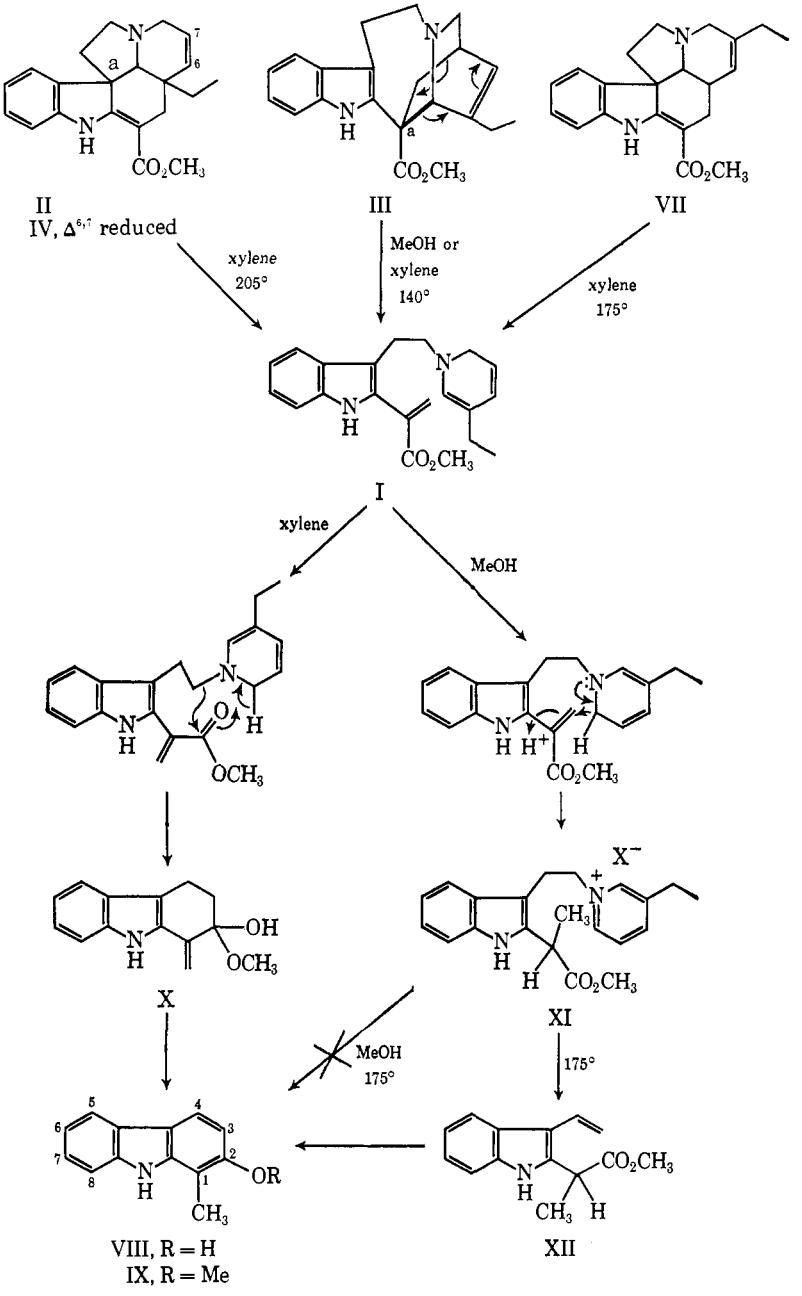
Further Observations on the Biogenetic-Type Chemistry of the Indole Alkaloids

Sir:

Our previous experiments[1,2] concerning the biosynthesis of the *Aspidosperma* and *Iboga* alkaloids from a *Corynanthe* precursor such as geissoschizine or corynantheine aldehyde in *Vinca rosea* have confirmed the original speculation[3] and the more specific predictions[4] with regard to the identity and oxidation level of the alkaloids involved, many of which had not previously been reported in *V. rosea*. Implicit in the detailed mechanistic proposals[4] is the intervention of the acrylic ester I which serves not only as an isomeric bridge between tabersonine (II) (*Aspidosperma*) and catharanthine (III) (*Iboga*) but also as a rationale for the appearance in nature of racemic alkaloids such as (±)-

(7) J. T. Edward, H. S. Chang, K. Yates, and R. Stewart, *Can. J. Chem.*, **38**, 1518 (1960).
(8) K. Yates and R. Stewart, *ibid.*, 37, 664 (1959).
(9) R. Stewart and K. Yates, *J. Am. Chem. Soc.*, **80**, 6355 (1958).
(10) R. Stewart and K. Yates, *ibid.*, **82**, 4059 (1960).
(11) A. Fischer, B. A. Gregor, J. Packer, and J. Vaughen, *ibid.*, **83**, 4208 (1961).

(1) A. A. Qureshi and A. I. Scott, *Chem. Commun.* 948 (1968).
(2) A. I. Scott, P. C. Cherry, and A. A. Qureshi, *J. Am. Chem. Soc.*, **91**, 4932 (1969).
(3) E. Wenkert and B. Wickberg, *ibid.*, **87**, 1580 (1965).
(4) A. I. Scott, 2nd Symposium on Natural Products, Mona, Jamaica, Jan 1968; A. A. Qureshi and A. I. Scott, *Chem. Commun.*, 945, 947 (1968); A. I. Scott, *Chimia*, **22**, 310 (1968).



vincadifformine (IV). Both reduced and dimeric modifications of type I have appeared recently in the alkaloids V[5] and VI,[6] respectively. The intermediacy of I has also been invoked in the biogenetic-type formation of racemic pseudocatharanthine (VII) and catharanthine (III) from tabersonine (II) by the action of acetic acid at elevated temperatures.[4,7]

It therefore became of interest to provide some evidence for the existence and stability of I or its close relatives in the chemistry of II and III and to search for more detailed mechanistic models for those biosynthetic processes[4] which have invoked I or closely related systems[3,5,6] as putative intermediates.

To this end, xylene solutions of the isomeric alkaloids (−)-tabersonine (II), (+)-catharanthine (III), and (±)-pseudocatharanthine (VII) were maintained in sealed tubes for 1.5 hr at the temperatures indicated. In each case (but with a different energy requirement) the same products were isolated and characterized as 3-ethylpyridine and 1-methyl-2-hydroxycarbazole (VIII): mp 221–225°; λ_{max} (EtOH), 216 (log ϵ 4.41), 238 (4.59), 252 (4.44), 256 (4.42 sh), 300 (4.13), 315 (3.87 sh), 328 nm (3.41 sh); nmr[8] (CD_3COCD_3) τ 2.05, 1 H, m (H-5); 2.22, 1 H, d, J = 8 Hz (H-4); 2.40–3.00, 3 *H*, *m* (H-6, -7, and -8); 3.15, 1 H, d, J = 8 Hz (H-3); 6.75, 1 H, s, exchanges (OH); 7.53, 3 H, s (CH_3); mass spectrum: base peak *m/e* 197.

We suggest that the formation of these products takes place by way of a retro-Diels–Alder reaction to afford the fugitive ester I followed by an intramolecular re-

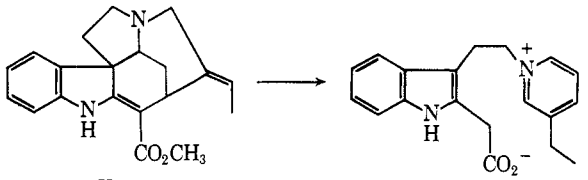
(5) P. A. Crooks, B. Robinson, and G. F. Smith, *Chem. Commun.*, 1210 (1968).

(6) D. A. Evans, G. F. Smith, G. N. Smith, and K. S. J. Stapleford, *ibid.*, 859 (1968). No stereochemical details are yet available for these and related[5] alkaloids, but they might well exist in racemic form if generated nonspecifically from I.

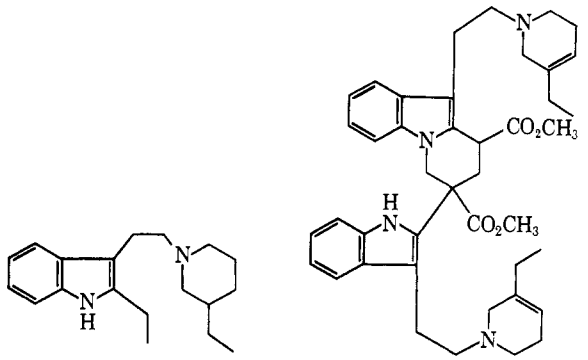
(7) It has been observed that below 180° in acetic acid solution only the bonds marked a in II and III are cleaved to afford *optically active* stereoisomers and structural isomers of II and III. Details of the latter processes will be discussed elsewhere. Similar results have been obtained by Professor J. Poisson (private communication).

(8) s = singlet; d = doublet; t = triplet; m = multiplet.

arrangement and hydrogen transfer from the dihydropyridine to the acrylic ester function yielding the hemiketal X with loss of 3-ethylpyridine as indicated. Elimination of methanol and further rearrangement then give the carbazole VIII. In support of the latter process 1-methyl-2-methoxycarbazole (IX) could be detected and characterized as a minor product of the reaction.



XIV XIII



V VI

More direct evidence for the formation of I was obtained by the capture in 50% yield of the racemic salt XI when catharanthine was heated in methanol at 140° for 2 hr. The pyridinium salt had λ_{max} (EtOH) 219, 269, 283 (sh), 291 nm; $[\alpha]_{300-600}$ 0° (EtOH); nmr[8] (D_2O) τ 1.7–3.3, 8 H, m (Ar–H); 5.30 and 6.66, 4 H, 2t ($-CH_2CH_2-$); 6.12, 1 H, q, J = 7.5 Hz ($CH(CH_3)CO_2CH_3$); 6.33, 3 H, s (CO_2CH_3); 7.55, 2 H, q, J = 7.5 Hz (CH_2CH_3); 8.62, 3 H, d, J = 7.5 Hz ($CH(CH_3)CO_2CH_3$); 9.18, 3 H, t, J = 7.5 Hz (CH_2CH_3).

In contrast to the intramolecular formation of the carbazole from the dihydropyridineacrylic ester I in the aprotic solvent xylene, the availability of solvent protons in the latter case appears to divert the collapse of this intermediate in methanol *via* an ionic mechanism to the pyridinium salt XI.[9] This salt is stable in methanol at 175° but on pyrolysis at this temperature affords the carbazole VIII, presumably *via* elimination of ethylpyridine and cyclization of the resulting vinyl ester XII. The generation of I in methanol solution could also be rationalized by an ionic mechanism[4] which recalls the formation of the betaine XIII from akuammicine (XIV).[10] Since the species I and XI could be reached *in vivo* from stemmadenine,[4] tabersonine (II), and catharanthine (III), it will be of interest to test these three alkaloids as biochemical precursors for V and VI and also to consider the system I $\rightleftarrows$ XI as a labile but isolable biosynthetic intermediate for the *Aspidosperma* and *Iboga* alkaloids. These experiments also provide a mechanistic rationale for the previous *in vitro* transformations[4] which have been found to be particularly sensitive to the temperature employed in the reaction[7] and where merging electrocyclic and ionic mechanisms may be operating.

(9) When the reaction is carried out in CH_3OD solution, the nmr spectrum of the salt no longer shows a signal at τ 6.12 ($CD(CH_3)CO_2CH_3$) and the doublet at τ 8.62 ($CH(CH_3)CO_2CH_3$) is replaced by a singlet (3 H). These observations are in accord with the mechanism I → XI.

(10) P. N. Edwards and G. F. Smith, *J. Chem. Soc.*, 1458 (1961).

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Received June 26, 1969

Biogenesis of *Strychnos*, *Aspidosperma*, and *Iboga* Alkaloids. The Structure and Reactions of Preakuammicine

Sir:

In the course of biosynthetic and biogenetic investigation of the indole alkaloid family, models have been devised[1-3] to simulate the *Corynanthe* → *Strychnos* → *Aspidosperma* → *Iboga* transformations. However the information revealed by these and related feeding experiments[4,5] still leaves unanswered both the nature of the intermediates between geissoschizine (I) (*Corynanthe*), akuammicine (II) (*Strychnos*), and stemmadenine (III) ("*Corynanthe–Strychnos*") and the mechanisms connecting them. It has been suggested[6] that a key member of this family situated at the main branching point of the pathway would be a prototype (IV) of the *Strychnos* alkaloids *retaining all ten of the original geraniol* carbon atoms which could suffer irreversible loss of a single carbon function to the "C_9" alkaloids, *e.g.*, akuammicine (II) and strychnine, or by a series of rearrangements generate the *Aspidosperma* and *Iboga* alkaloids. Such a model was demonstrated in the laboratory and detailed suggestions made implicating stemmadenine (III) as a key intermediate for this latter process.[3] We now describe the isolation and properties of a new alkaloid, *preakuammicine*, for which the long sought structure IV is proposed and which, from its position in the *Vinca* sequence, meets at least one of the criteria as an intermediate. Furthermore the chemistry of IV provides *in vitro* analogy for its presumptive role as a true biointermediate.

Careful separation by repeated tlc of the alkaloidal fraction of 42–48-hr-old seedlings of *Vinca rosea* afforded material with homogeneous tlc behavior (R_f 0.41 in 20% $CHCl_3$–MeOH; silica gel G). The amorphous alkaloid preakuammicine, $C_{21}H_{24}N_2O_3$ (IV), obtained in this way was characterized as an indolenine: λ_{max}^{EtOH} 262 nm (ϵ 6000), changing on storage at 20° to λ_{max} 292, 325 nm (chromophore II); nmr ($CDCl_3$) τ 2.2–3.0 m (Ar–H); 4.7 q ($CH_3CH=$); 6.05 s (CH_2OH); 6.15 s (CO_2CH_3); 8.45 d ($CH_3CH=$); mass spectrum (rela-

(1) A. A. Qureshi and A. I. Scott, *Chem. Commun.*, 945 (1968).
(2) A. A. Qureshi and A. I. Scott, *ibid.*, 947 (1968).
(3) A. I. Scott, *Chimia*, 22, 310 (1968).
(4) A. I. Scott, 2nd Symposium on Natural Products, Mona, Jamaica, Jan 1968.
(5) A. A. Qureshi and A. I. Scott, *Chem. Commun.*, 948 (1968).
(6) E. Wenkert and B. Wickberg, *J. Am. Chem. Soc.* **87**, 1580 (1965); *cf.* A. R. Battersby, *Pure Appl. Chem.*, **14**, 117 (1967); *Chimia*, **22**, 313 (1968).