enediaminetetraacetato-cuprate(II), CuY^{-2}

$$NiT^{+2} + CuY^{-2} \longrightarrow CuT^{+2} + NiY^{-2}$$

is found to proceed by a chain reaction mechanism. This, we believe, is the first example of a chain reaction in aqueous solution caused by coördination substitution reactions.

The NiT^{+2} and CuY^{-2} complexes are both extremely slow in their dissociation reactions (substitution by water) in neutral solution.[1,2] Yet, the exchange reaction between these complexes occurs readily. The reaction is initiated by the trace concentration (approx. 10^{-6} M) of free triethylenetetramine ($T_T = H_3T^{+3} + H_2T^{+2} + HT^{+} + T$) which is in equilibrium with the complex.

$$NiT^{+2} \rightleftharpoons Ni^{+2} + T_T$$

This trace of T_T attacks the CuY^{-2} complex, greatly accelerating the rate of EDTA displacement. The trace of EDTA liberated in turn attacks the NiT^{+2} greatly accelerating the rate of triethylenetetramine displacement. Thus, the chain propagating steps are

$$T_T + CuY^{-2} \rightleftharpoons CuT^{+2} + Y_T$$
$$Y_T + NiT^{+2} \longrightarrow NiY^{-2} + T_T$$

Traces of metal ions which can complex triethylenetetramine or EDTA act as chain inhibitors. The Ni^{+2} may act as a chain terminator by the reactions

$$Ni^{+2} + T_T \longrightarrow NiT^{+2}$$
$$Ni^{+2} + Y_T \longrightarrow NiY^{-2}$$

Slight excesses of either ligand greatly increase the exchange rate as expected by this mechanism. The observed kinetic orders with excess CuY^{-2} or NiT^{+2} support the mechanism.

Thus when an excess of NiT^{+2} is present the reaction rate is proportional to $[CuY^{-2}][NiT^{+2}]^{1/2}$ while with an excess of CuY^{-2} present the reaction rate is proportional only to $[NiT^{+2}]^{1/2}$ at high pH and has a more complex dependence at lower pH. These reaction orders are consistent with the proposed mechanism and the detailed kinetic arguments as well as the evaluation of the individual rate constants will be published. Furthermore, the chain initiating step and the chain terminating step both may be eliminated from the exchange rate by the addition of an excess of either trien or EDTA. Under these conditions with excess NiT^{+2} the rate is proportional to $[T_T]_{added}$ $[CuY^{-2}]$ and with excess CuY^{-2} the rate is proportional to $[Y_T]_{added}$ $[NiT^{+2}]$.

Chain reaction mechanisms for metal complex–metal complex exchange reactions should be expected for many other systems when sufficient free ligand is available to increase the dissociation rates of the complexes. Multidentate ligand complexes should be particularly susceptible to this type of reaction because their dissociation rates are slower and lower concentrations of the ligands are needed to accelerate their displacement of one another than is the case for lower dentate ligands.

DEPARTMENT OF CHEMISTRY D. C. OLSON
PURDUE UNIVERSITY D. W. MARGERUM
LAFAYETTE, INDIANA

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BIOSYNTHESIS IN THE AMARYLLIDACEAE. THE INCORPORATION OF 3-C^{14}-TYROSINE IN SPREKELIA FORMOSISSIMA

Sir:

Previous biogenetic experiments with plants of the family *Amaryllidaceae* have been concerned largely with the origin of the C_6-C_2 fragment which elaborates the hydroaromatic ring C and the 5-membered ring D in many alkaloids. Experimental evidence has been obtained for the incorporation of both 2-C^{14}-tyrosine[1-3] and 1-C^{14}-norbelladine[3-5] by various plants within the family to afford alkaloids shown in several cases to be labelled solely at the expected position.

We have been concerned with possible precursors of the C_6-C_1 unit in the *Amaryllidaceae* alkaloids which is represented by the aromatic ring A and the benzylic carbon adjacent to the basic nitrogen. Feeding 3-C^{14}-tyrosine to the stems of flowering *Sprekelia formosissima* gave rise to radioactive haemanthamine (I, R = H) (isolated by dilution with inactive alkaloid), haemanthidine (I, R = OH) (0.20% incorporation), and tazettine (II) (0.16% incorporation). Based on previous biosynthetic experiments,[3] it was anticipated that radioactivity would be found at the carbon atoms of I (R = H or OH) and II at the positions marked by the asterisk. If 3-C^{14}-tyrosine were to serve also as a precursor of ring A and the benzylic carbon (C_6 in I and C_8 in II), radioactivity at the position marked by the dagger would be expected in addition.

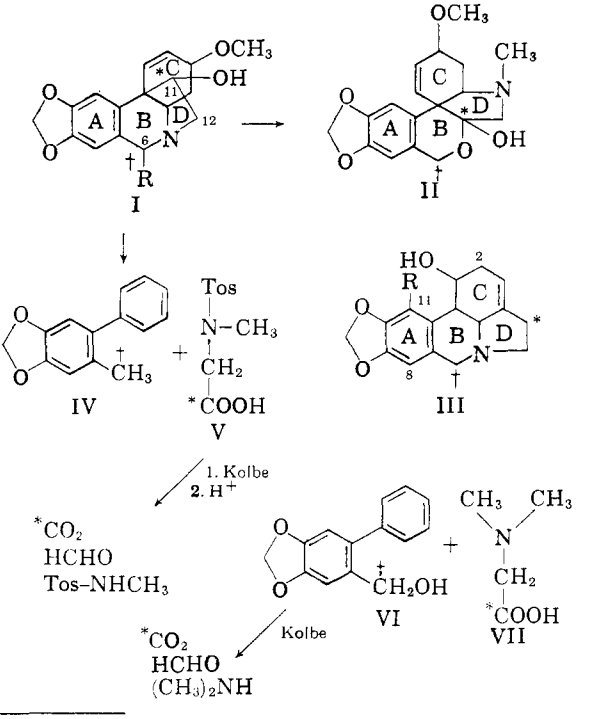

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TABLE I

RELATIVE SPECIFIC ACTIVITIES OF THE ALKALOIDS AND THEIR DEGRADATION PRODUCTS[a]

Compound	Activity	Compound	Activity	Compound	Activity
Haemanthamine (I, R = H)	1.00	Haemanthidine (I, R = OH)	1.00	Tazettine (II)	1.00
Oxohaemanthamine	1.00	Tazettine (II)	1.04	Tazettine methiodide	0.97
2-Methyl-4,5-methylenedioxybiphenyl (IV)	0.00	Tazettine methiodide	1.04	6-Phenylpiperonyl alcohol (VI)	0.00
N-Tosylsarcosine (V)	1.00	6-Phenylpiperonyl alcohol (VI)	0.00	Dimethylglycine hydrochloride (VII)	0.95
Formaldehyde dimethone	0.00	Dimethylglycine hydrochloride (VII)	1.06	Carbon dioxide	0.95
Methanol 3,5-dinitrobenzoate	0.00	Formaldehyde dimethone	0.00	Formaldehyde dimethone	0.00
Carbon dioxide	0.9[b]	Carbon dioxide	1.00	N,N-Dimethyl-*p*-toluenesulfonamide	0.00
		N,N-Dimethyl-*p*-toluenesulfonamide	0.00		

[a] Samples were counted in a Packard Tri-Carb Scintillation Counter in toluene or dioxane-napthalene scintillator solutions. The carbon dioxide was collected directly from the Kolbe reaction in hyamine hydroxide 10-X and counted in toluene. [b] Based on obtaining 78% of the counts compared to a model run which yielded 87%.

Degradation of haemanthamine (I, R = H) by methods outlined earlier[3] has revealed that *all* the radioactivity in this alkaloid resides at C_{11}. The degradation product, 2-methyl-4,5-methylenedioxybiphenyl (IV), which represents rings A, C, and the benzylic carbon, is totally inactive. To corroborate this finding, radioactive haemanthidine (I, R = OH) was converted to tazettine[6] and then degraded by the Hofmann method[7] to 6-phenylpiperonyl alcohol (VI) and dimethylglycine hydrochloride (VII). The same degradation was applied to the radioactive tazettine isolated from the plants. In both cases, the 6-phenylpiperonyl alcohol was completely inactive. Kolbe electrolysis[3] of the dimethylglycine hydrochloride provided radioactive carbon dioxide and inactive formaldehyde isolated as the dimethone derivative,[3] indicating that 3-C^{14}-tyrosine or a close biological equivalent can serve as a precursor of ring C and the two-carbon chain of ring D with no scrambling of the label.[8] Table I lists relative activities of the degradation products of these alkaloids.

These data show that either a C_6-C_1 unit is not the precursor of ring A and the benzylic carbon atom of haemanthamine, haemanthidine, and tazettine, or that, if such a unit is the precursor, it cannot be derived from tyrosine in *S. formosissima*. This is in contrast to the results of Suhadolnik and Fischer[9] who showed that 3-C^{14}-phenylalanine is a precursor of ring A and the benzylic carbon of lycorine (III, R = H; OH at C_2). Further work will be required to establish whether these results are a reflection of different biosynthetic pathways for 5,10b-ethanophenanthridine alkaloids and those of the lycorine type. However, there have been recent indications of some differences in that the aromatic substitution pattern[10] of falcatine (III, R = OCH_3) is as expected from biogenetic theory[11] whereas that of the powellane alkaloids[12] requires a rearrangement step. The biosynthetic inter-relationships of alkaloids in this series are being further studied.

Acknowledgment.—We are grateful to Dr. R. Binks for help with the extraction work and to Dr. P. W. Jeffs for kindly informing us of his incorporation of 3-C^{14}-tyrosine into haemanthamine (without scrambling).

(6) For one method of conversion of haemanthidine to tazettine, see H.-G. Boit and W. Stender, *Chem. Ber.*, **89**, 161 (1956).

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(8) Strictly, these results prove that ring C and the asterisked carbon of ring D can be derived from tyrosine. However, our earlier work[3] established incorporation of the carbon atoms from position 2 of tyrosine into position 12 of haemanthamine. That the C_6-C_1 unit is incorporated intact in all three alkaloids is supported by the isolation of radioactive haemanthamine, haemanthidine, and tazettine from *S. formosissima* fed with 2-C^{14} tyrosine.

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LABORATORY OF CHEMISTRY OF NATURAL PRODUCTS
NATIONAL HEART INSTITUTE — W. C. WILDMAN
BETHESDA 14, MD. — H. M. FALES
THE UNIVERSITY — A. R. BATTERSBY
BRISTOL, ENGLAND

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STEREOCHEMICAL REQUIREMENTS OF MULTIPLE REARRANGEMENTS. EVIDENCE FOR CLASSICAL CARBONIUM ION INTERMEDIATES

Sir:

Although the importance of non-classical, mesomeric carbonium ions as intermediates in Wagner–Meerwein rearrangements has been stressed in recent years, the mechanistic role played by the classical, non-mesomeric species has not been made clear. We report here some experimental evidence that implies the presence of *both* classical and non-classical ions in a case of multiple rearrangement.

Nitrous acid deamination of *endo*-2-aminomethylnorbornane I previously[1,2] had been shown to give mostly *endo*-(*equatorial*)-bicyclo[3.2.1]octanol-2 II and a little of the *exo*-(*axial*)-isomer III. Using

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