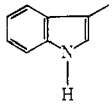
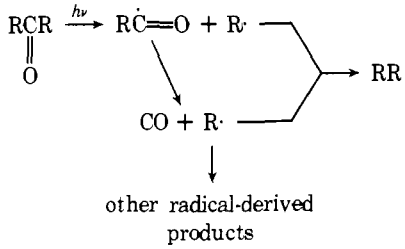
Table I. Thermal Decarbonylation of $(OC)_9Co_3CC(O)R$ Complexes

| R in $(OC)_9Co_3CC(O)R$ | Reaction time, h | $(OC)_9Co_3CR$, % yield |
|---|---|---|
| $p$-$Me_2NC_6H_4$– | 0.75 | 70 |
| $p$-$MeC_6H_4$– | 6 | 69 |
| $C_6H_5$– | 5 | 66 |
| $p$-$BrC_6H_4$ | | 0[a] |
|  | 2 | 63 |
|  | 3 | 71 |
|  | 10 | 47 |
| $C_2H_5$– | 18 | 46[b] |
| $Me_2CH$– | 4 | 31[b] |
| $n$-$C_4H_9$– | 20 | 42[b] |
| $Me_3C$– | | 0 |

[a] No decarbonylation product was formed; partial recovery of starting material with complete decomposition of remaining complex. [b] Lower yields of alkyl complexes probably reflect their lower thermal stability.

This thermal decarbonylation of ketones is very unusual and finds its closest formal parallel in the Norrish type I photochemical fragmentation of ketones in the gas phase and, less commonly, in solution (eq 2). For instance, in the photo-




(2)

chemical decomposition of dibenzyl ketone in solution such decarbonylation and radical coupling is the predominant process following $\alpha$-cleavage.[13]

The C–C bond linking the acyl or aroyl substituent to the $(OC)_9Co_3C$ cluster may well be rather weak as a result of steric factors involving the highly hindered cluster group. Thus a thermal homolytic cleavage of this bond is a conceivable process. However, other mechanistic possibilities which involve the $(OC)_9Co_3C$ unit more intimately may be conceived. Further mechanistic speculation is fruitless in the absence of further experimental information.

Finally, we note that medium effects can be important in reactions of $(OC)_9Co_3CC(O)R$ complexes. Thus ferrocenoylmethylidnetricobalt nonacarbonyl, which was for the most part decarbonylated on treatment with $H_2/CO$ in refluxing benzene and gave only a low yield of the alcohol, reacted to give the alcohol in 72% yield with no observable decarbonylation when this reaction was carried out in refluxing benzene containing about 4% by volume of glacial acetic acid.

It is clear that our understanding of these processes which are described above is at a very rudimentary stage. However, some very novel and interesting chemistry of $(OC)_9Co_3CC(O)R$ complexes has been uncovered which can have preparative utility within the cobalt cluster area.

**Acknowledgment.** We are grateful to the National Science Foundation (Grant No. MPS75-21215) for generous support of this research.

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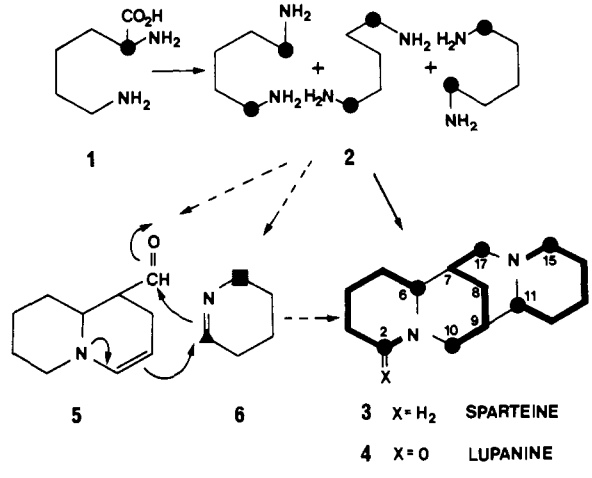
## The Biosynthesis of the Lupine Alkaloids. A Reexamination[1]

*Sir:*

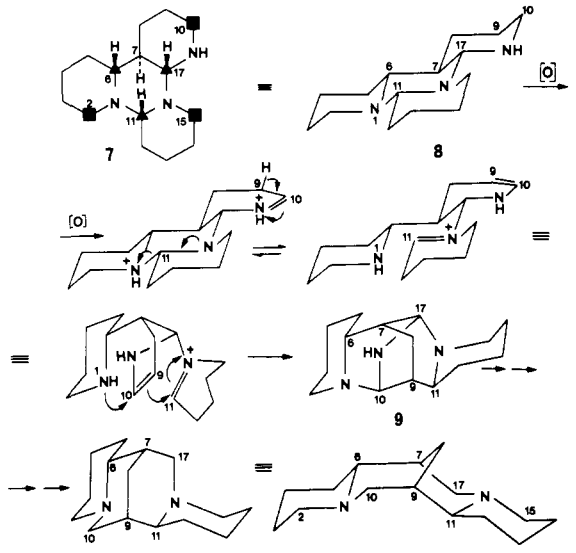
The $C_{15}$ lupine alkaloids, e.g., sparteine (**3**) and lupanine (2-oxosparteine) (**4**), originate from three $C_5$ fragments,[2,3] which are derived from lysine (**1**)[4,5] via cadaverine (**2**),[2-5] and are incorporated in symmetrical fashion and with equal efficiency into each of the three $C_5$-segments of the alkaloids. Thus, label from [2-$^{14}$C]lysine is equally distributed among six carbon atoms, C-2, 6, 10, 11, 15, and 17, of sparteine[4] and of lupanine.[5,6] The biogenetic anatomy of the alkaloids is usually[2,3] represented as shown in Scheme I.

The two nitrogen atoms are also supplied by lysine.[4,10] Two of the three $C_5$ fragments evidently maintain a lysine nitrogen, entering the alkaloids as $C_5N$ units, whereas the third $C_5$ fragment enters devoid of nitrogen.[11] Even so, it is likely, in view of the observed equal distribution of label from [2-$^{14}$C]lysine or [1-$^{14}$C]cadaverine among the three segments of

Scheme I. Incorporation of Lysine and Cadaverine into Sparteine



Scheme II. Sparteine as a Modified Trimer of $\Delta^1$-piperideine (numbering of carbon atoms in all formulas corresponds to the numbering in sparteine)



10 [≡(−)-3]

the alkaloid molecules,[2-5] that, at the time of their union, the three precursor fragments are identical.

Intermediates between cadaverine and the alkaloids have not been identified. The key step in the biogenetic process is assumed[12] to be the union of the quinolizidine derivative (**5**) with $\Delta^1$-piperideine (**6**). Several hypothetical pathways leading from cadaverine **2** to **5** have been proposed. One of these[13] invokes condensation of two different oxidation products of cadaverine, 5-aminopentanal (the open-chain form of $\Delta^1$-piperideine (**6**)), and glutardialdehyde, followed by reduction to yield a product from which the skeleton of **5** is generated by intramolecular Mannich reaction.[14] Another scheme[17] postulates intermediacy of tetrahydroanabasine, the dimer of $\Delta^1$-piperideine, on route to **5**.

Neither of these two variants of the path to sparteine via **5** impose the stereochemical restrictions which appear to be inherent in the structure of the naturally occurring lupine alkaloids: In many cases both enantiomers of a given alkaloid occur in nature (e.g., (−)-(6*R*:7*S*:9*S*:11*S*)- and (+)-(6*S*:7*R*:9*R*:11*R*)sparteine). Yet, with the single exception of (−)-$\beta$-isosparteine (6*R*:7*R*:9*R*:11*R*), the relative configuration of all lupine alkaloids, which contain chiral centers both at C-6 and C-11, is such that the hydrogen atom at C-6 is cis to the central methylene bridge (C-8), whereas the hydrogen at C-11 can be either cis or trans (e.g., (+)-lupanine (6*R*:7*S*:9*S*:11*S*) and (+)-$\alpha$-isolupanine (6*R*:7*S*:9*S*:11*R*)).[18,19]

We now present some evidence in support of a new biogenetic hypothesis which can account for these observations. It is our view that the $C_{15}$ lupine alkaloids are modified trimers of $\Delta^1$-piperideine. One of these trimers is isotripiperideine (**7**).[20] A favored stereoisomer of this compound is the all-trans enantiomeric pair (6$\beta$, 7$\alpha$, 11$\beta$, 17$\beta$) (**8**) in the all-chair conformation. It is from this stereoisomer that the alkaloid skeleton with the configurations found in the $C_{15}$-lupine alkaloids (other than $\beta$-isosparteine) can be derived in four steps, via the "prealkaloid" trimer **9** (Scheme II). The stereochemistry of this trimer at three sites, C-6, C-7, and C-9, is determined by the stereochemistry of the isomer of isotripiperideine from which it is derived. The configuration at the fourth site (C-11) is determined in the course of ring closure, by the direction (re or si) of the intramolecular attack at C-11.

Removal of the unwanted central nitrogen, by elimination, by displacement, or oxidatively, yields the skeleton[21] from which the "cis" lupine-alkaloids are derived: One enantiomer of the piperideine trimer (**8**) yields the 6*R*:7*S*:9*S*:11*S* (e.g., (−)-sparteine (**10**)) and 6*R*:7*S*:9*S*:11*R* (e.g., (−)-$\alpha$-isosparteine) alkaloids. The other enantiomer yields the alkaloids of the 6*S*:7*R*:9*R*:11*R* (e.g., (+)-sparteine) and of the 6*S*:7*R*:9*R*:11*S* series. (−)-$\beta$-Isosparteine (6*R*:7*R*:9*R*:11*R*), the only "trans" lupine alkaloid,[18,19] may be derived by analogous steps from another stereoisomer (6$\beta$, 7$\beta$, 11$\alpha$, 17$\alpha$) of isotripiperideine. Interestingly, the alternative product from this precursor, the (6*R*:7*R*:9*R*:11*S*) isomer, is identical with (+)-(6*S*:7*R*:9*R*:11*R*) sparteine.[22]

Table I. Distribution of Label from $\Delta^1$-Piperideine in Lupanine

| Product | C-atoms of lupanine | Precursor: $\Delta^1$-piperideine [2-$^{14}$C]- Relative molar specific activity | [6-$^{14}$C]- Relative molar specific activity |
|---|---|---|---|
| Lupanine (**4**) | All | 100 ± 1 | 100 ± 1 |
| 17-Oxosparteine from lupanine[5] | All | 101 ± 2 | 100 ± 1 |
| 17-Oxolupanine from lupanine[28] | All | | 100 ± 1 |
| Benzoic acid from lupanine[3] | C-2 | 1 ± 0.1 | 27 ± 1 |
| Benzoic acid from 17-oxosparteine[5] | C-17 | 27 ± 1 | 2 ± 0.2 |
| $\beta$-Alanine from 17-oxolupanine[28] | C-13, 14, 15 | 0.3 ± 0.7 | 33 ± 1 |
| $\gamma$-Aminobutyrate from 17-oxolupanine[28] | C-12, 13, 14, 15 | 0.3 ± 2 | 32 ± 1 |
| Pipecolic acid from 17-oxolupanine[28] | C-9, 11, 12, 13, 14, 15 | 33 ± 1 | 32 ± 1 |

We have tested this hypothesis. In separate experiments [2-$^{14}$C]- and [6-$^{14}$C]-$\Delta^1$-piperideine[26] (**6**) were administered by the wick method to 3-month old plants of *Lupinus angustifolius* L. The plants were kept in contact with tracer for 3 days, and lupanine (**4**) (specific activity, $4.4 \times 10^6$ and $2.2 \times 10^7$ dpm per mmol, respectively) was then isolated by standard methods.[5] The labeled product was diluted with carrier (ca. 40-fold) and degraded by reaction sequences which permitted assay of radioactivity at C-2 (benzoic acid),[3] at C-17 (benzoic acid),[5] at C-15 ($\beta$-alanine, $\gamma$-aminobutyric acid),[28] and at C-11 (pipecolic acid minus $\beta$-alanine).[28]

The results (Table I) are in keeping with the new hypothesis. The observed labeling pattern of lupanine is as predicted for the route to the alkaloids from $\Delta^1$-piperideine (**6**) via isotripiperideine (**7**). Carbon-2 of $\Delta^1$-piperideine (▲ in **6**) supplies C-17, C-11, and, by inference, C-6 of lupanine (**4**)*while carbon-6 of $\Delta^1$-piperideine (■ in **6**) yields C-2, C-15, and, by inference, C-10 of lupanine.

**Acknowledgment.** This work was supported by the National Research Council of Canada.

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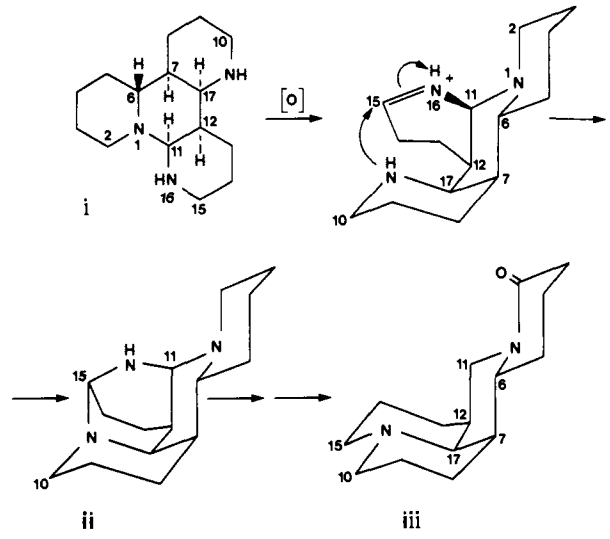
(21) That a compound other than sparteine is the primary alkaloidal product of the biosynthetic sequence is indicated by the finding[9] that sparteine is not an intermediate in the formation of lupanine. The structure of the primary intermediate demanded by the new hypothesis is closely related to 17-oxosparteine or to 10-oxosparteine (aphylline), both of which are naturally occurring compounds.[18,19]
(22) The hypothesis is also applicable to the alkaloids of the matrine series. The piperideine trimer from which these bases are derivable is aldotripiperideine (i),[11,23,24] a compound which has been isolated from a plant source.[25] The route from the required stereoisomer of aldotripiperideine (i) to matrine (iii) via the "prematrine" trimer (ii) is shown below. Matrine as a modified trimer of $\Delta^1$-piperideine (numbering of carbon atoms in all formulas corresponds to the numbering in sparteine).

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(30) On leave of absence from the Department of Organic Chemistry, University of Warsaw, Poland.

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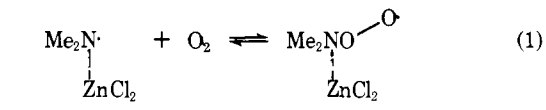
## Radical Catalyzed Epoxidation with Oxygen[1]

*Sir:*

We wish to report the following reactions of oxygen, catalyzed by amino radicals complexed with zinc chloride. Under

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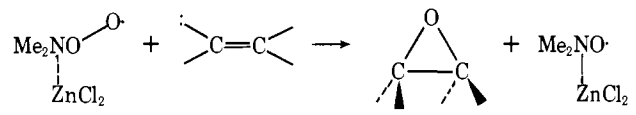
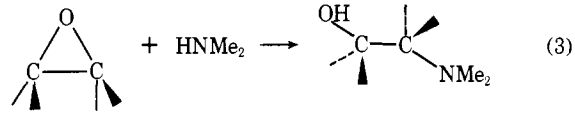
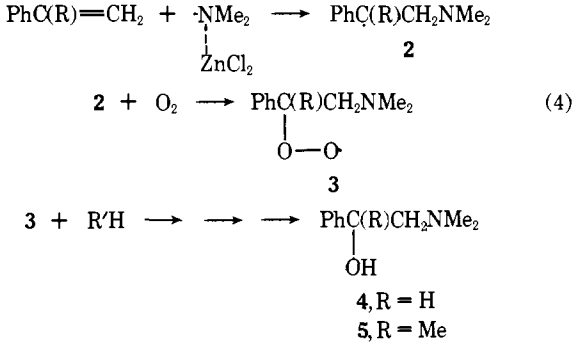



the experimental conditions used, these reactions were usually followed by a third. The case for the unique reactions (eq 1 and




2) rests on the following observations and arguments. Tetramethyl-2-tetrazene (TMT) in dry THF solution was mixed with an excess of anhydrous $ZnCl_2$ and the appropriate olefin. The mixture was warmed at 40–50 °C from 5 to 10 h under a stream of oxygen. The reaction mixture was separated by acid extraction (1 M HCl) of the basic products[2] and fractionation of these by GLC. The components of this fraction were subjected to mass spectral and NMR analysis.[3] The reaction of styrene and $\alpha$-methylstyrene gave the amino alcohols **4** and **5**, respectively, in 30–40% yields.

These products are consistent with the following (eq 4). The reactions (eq 4) have precedent in the mechanism proposed by Minisci and Galli[4] to explain their results on addition of redox generated amino radicals to alkenes in presence of oxygen.




Mechanism 4, however, does not explain the behavior of the other alkenes studied. Indene gave two amino alcohols, *trans*-2-dimethylamino-1-indanol (**6**)[5] and *trans*-1-dimethylamino-2-indanol (**7**)[6] in 5–10% yields, each. While amino alcohol **6** is consistent with mechanism 4, the amino alcohol **7** is not, because it would require the addition of the amino radical to the benzylic position, an energetically unfavorable site. The reaction of *trans*-$\beta$-methylstyrene produced, *exclusively*, *erythro*-1-dimethylamino-1-phenyl-2 propanol (**8**). This reaction was both regio- and stereospecific. The products from *cis*-$\beta$-methylstyrene were *threo*-1-dimethylamino-1-phenyl-2-propanol (**9**) and *threo*-2-dimethylamino-1-phenyl-1-propanol (**10**). Again, the reaction was stereospecific but, in this case, not regiospecific. In the case of the $\beta$-methylstyrenes only amino alcohol **10** is consistent with mechanism 4.

All of the "abnormal" products can be accounted for if it is assumed that they are formed by reaction 3. Thus, treatment of indene oxide with dimethylamine gave **7**, *trans*-$\beta$-methyl-