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A REMARKABLE OXIDATIVE FRAGMENTATION OF 16-EPI-19-S-VINDOLININE

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Abstract — An interesting oxidative fragmentation of the hexacyclic 16-epi-19-S-vindolinine (1) to the tricyclic product (6) is reported.

We have recently described the isolation and structure of 16-epi-19-S-vindolinine (1), a new dihydroindole alkaloid from the leaves of *Catharanthus roseus.*[1] The substance presents an intriguing hexacyclic structure,and it appeared of interest to investigate procedures for the cleavage of C_2-C_{19} bond. We report here a remarkable reaction which not only cleaves the C_2-C_{19} bond but also results in a fragmentation of the piperidine ring resulting in the facile transformation of the hexacyclic (1) to the tricyclic product (6) in one step on oxidation with lead tetraacetate.

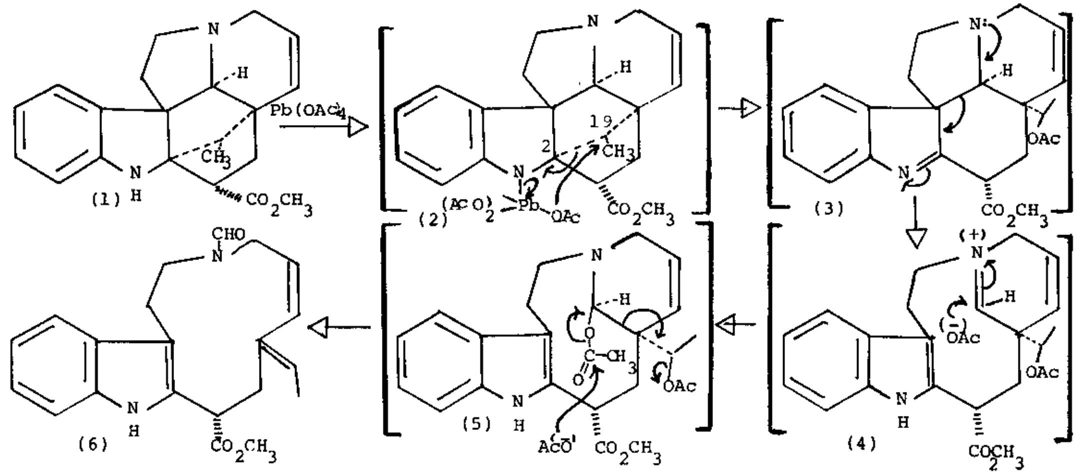
16-Epi-19-S-vindolinine,when refluxed in benzene for 3 h in the presence of an equimolar amount of lead tetraacetate, was found to be smoothly transformed to two faster running products. The major product formed in ∿70% yield afforded a normal indolic U.V. spectrum. The I.R. spectrum (KBr) showed bands at 1655 cm^{-1} and 1730 cm^{-1}, which were assigned to N_b-CHO and - CO_2CH_3 groups respectively. The mass spectrum showed M^+ at 352.1783 (calc. for $C_{21}H_{24}N_2O_3$, 352.1786) and other major peaks at 320, 293, 214, 169 and 154. The PMR spectrum ($CDCl_3$) showed resonances at δ 1.23, (3H, d, J=5.6Hz, $>C=CH-C\underline{H}_3$), δ 3.67 (3H, s, $OC\underline{H}_3$), δ 5.46 (1H, q, J=5.6Hz, $>C=C\underline{H}-CH_3$), δ 5.7-6.1, (2H, m., $\underline{H}C=C\underline{H}$), δ 7.6-6.9 (4H, m, aromatic), δ 8.00 (1H, s, N_b-$C\underline{H}O$) and δ 8.35 (1H, s, $N\underline{H}$). Irradiation at δ 5.46 resulted in the collapse of the methyl group at δ 1.23 to a singlet.

The above spectroscopic data were identical with those for (6), a product previously reported to be formed from 19-iodo-tabersonine on heating with sodium acetate in DMF.[2] In order to confirm the structure of the oxidation product, 16-epi-19-S-vindolinine (1) was oxidized with iodine under conditions previously described for the oxidation of its diastereoisomer.[3] This afforded the corresponding 19-iodo-tabersonine in quantitative yields. Treatment of the latter with sodium acetate in hot DMF afforded (6). A direct spectroscopic and chromatographic comparison of the product formed by lead tetraacetate oxidation with that prepared from 19-iodotabersonine[2] unambiguously established its structure. A plausible mechanism for the formation of (6) is presented in Scheme (1).

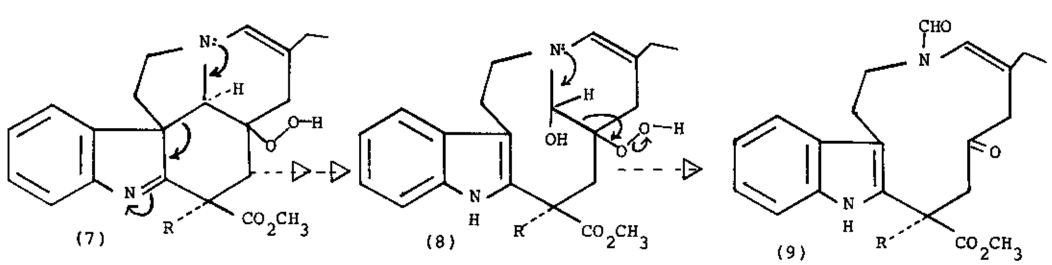
The second minor product formed in the lead tetraacetate oxidation possessed a U.V. characteristic for the dihydroindole system. Further work on the structure of this material is under progress.

The facile formation of (6) from (1) is biogenetically interesting particularly in view of the occurrence of the binary indole alkaloids such as catharine (9)[4] in which one of the moieties bears a distinct resemblance to (6). This raises the interesting possibility that the indole moiety of catharine may arise by a parallel process occurring in a binary precursor alkaloid such as (7), Scheme (2).

SCHEME (1)



SCHEME (2) (R=10-vindolinyl)



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