Application of a New Reaction of α-Phenylselenylketones to the Synthesis of Erysotrine

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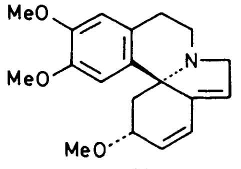
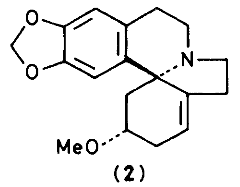
Treatment of an α-phenylselenylketone with mercury(II) perchlorate in methanol yielded an α,α-dimethoxyketone; by using this new reaction an erythrinan alkaloid, erysotrine, was synthesized.

Erysotrine (**1**) or its 8-oxo-derivative, erysotramidine, which are erythrinan alkaloids of the dienoid type, have been synthesized by three routes.[1—3] Here we present a new synthesis of these alkaloids by a completely different route which utilizes a new carbonyl transposition reaction *via* phenylselenylation. Our present work not only completes the synthesis of the above alkaloids but also provides a general route to the alkaloids of alkenol type such as erythramine (**2**) and isococculidine (**3**).

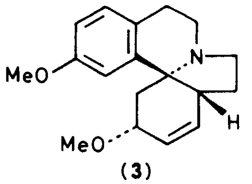
The synthesis was started with the 1,7-cycloerythrinan derivative (**5**),† m.p. 183—184 °C, which is easily prepared



(1)



(2)



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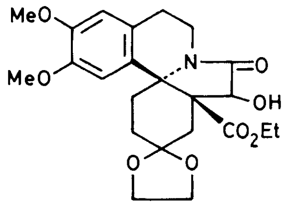

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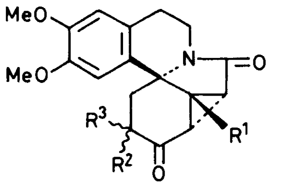
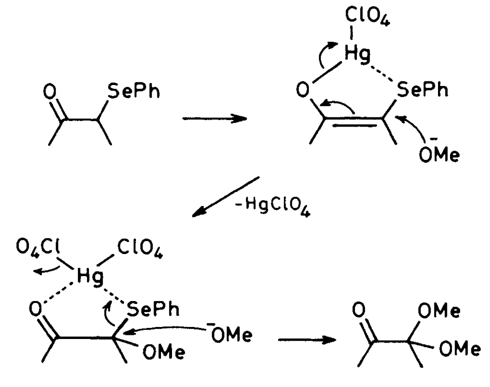
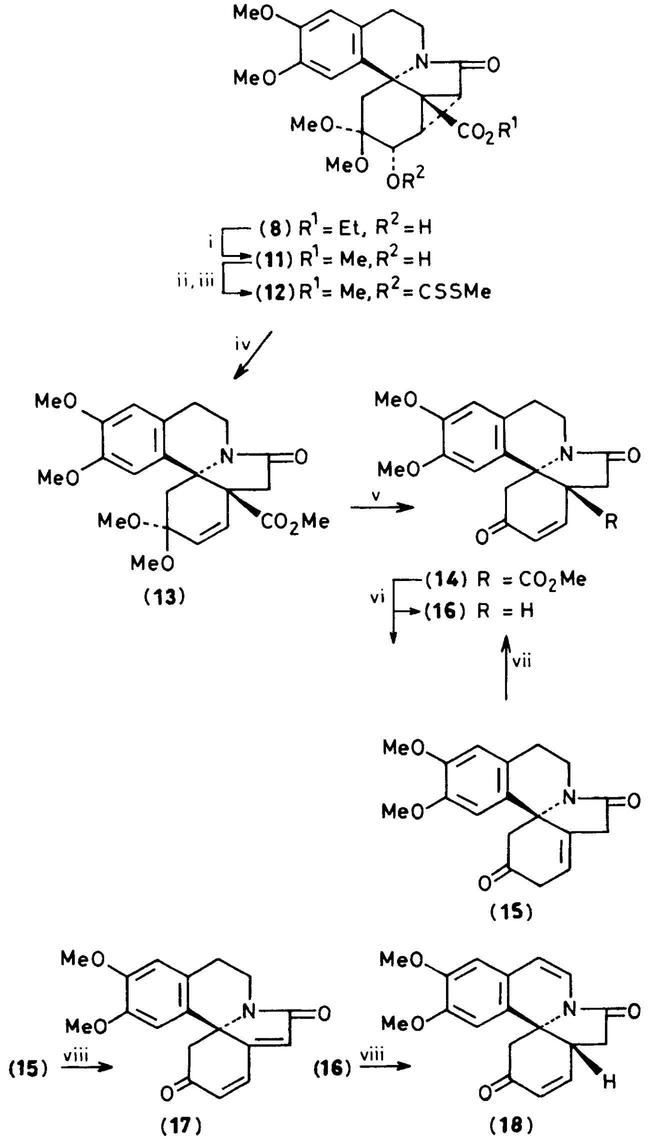


(**5**) $R^1 = CO_2Et$, $R^2 = R^3 = H$
(**6**) $R^1 = CO_2Et$, $R^2 = H$, $R^3 = SePh$
(**7**) $R^1 = CO_2Et$, $R^2 = R^3 = OMe$
(**9**) $R^1 = R^2 = H$, $R^3 = SePh$
(**10**) $R^1 = H$, $R^2 = R^3 = OMe$



Scheme 1



Scheme 2. *Reagents and conditions:* i, NaOMe, MeOH; ii, NaH; iii, CS$_2$, MeI, imidazole; iv, Bu$_3$SnH, reflux in toluene, 3 h; v, 1% HCl–acetone, 50 °C; vi, CaCl$_2$ [gives 5 : 1 (**15**) : (**16**), (83%)] or MgCl$_2$ [gives 1 : 1 (**15**) : (**16**), (55%)], Me$_2$SO, 140 °C, 2 h; vii, heat, 1,8-diazabicyclo[5.4.0]undec-7-ene, benzene; viii, 2,3,5,6-dichlorodicyanobenzoquinone, dioxane.

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† All new compounds in this communication gave satisfactory elemental analyses and/or mass spectra, and other spectral data (n.m.r. and i.r.).

from 2-ethoxycarbonyl-4,4-ethylenedioxycyclohexanone *via* the known erythrinan derivative (**4**)[4] (overall yield 69%).

The key step of this synthesis, introduction of a carbonyl function α to the original ketone, was achieved as follows. Treatment of (**5**) with PhSeCl and a catalytic amount of $BF_3 \cdot Et_2O$ in tetrahydrofuran (reflux, 3.5 h) afforded a gummy phenylselenide (**6**) which on treatment with mercury(II) perchlorate (2 equiv.) in methanol gave the α,α-dimethoxyketone (**7**), as a gum. This was characterized as the crystalline 2α-alcohol (**8**), m.p. 189—191 °C, after borohydride reduction, 55% from (**5**). Application of the above Hg^{2+} treatment to (**9**) yielded the corresponding dimethoxyketone (**10**), m.p. 209—212 °C, in 90% yield, indicating the generality of this new oxidative methoxylation reaction. We suggest that the reaction proceeded as shown in Scheme 1.

Transesterification of (**8**) with sodium methoxide in methanol yielded the methyl ester (**11**) (92%), m.p. 211—212 °C, which was converted into the dithiocarbonate (**12**) (81%), m.p. 205—206 °C, treatment of which with tributyltin hydride yielded the deoxy-olefin (**13**) (97%), m.p. 194—196 °C, with concomitant opening of the cyclopropane ring. Acid hydrolysis of (**13**) gave the enone (**14**) (100%), m.p. 206—207 °C. Heating of this with calcium chloride in dimethyl sulphoxide resulted in demethoxycarbonylation to yield the enones (**15**) and (**16**) in a ratio of 5 : 1 (83%), while the reaction with magnesium chloride[5] gave (**15**) and (**16**) in a ratio of 1 : 1 (55%). Compound (**15**) readily isomerized to (**16**) on heating with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene (Scheme 2). These enones are potential intermediates in the preparation of the alkenol type erythrinan alkaloids.

The enone (**15**) was oxidized with 2,3,5,6-dichlorodicyanobenzoquinone (DDQ) in dioxane to the dienone (**17**) (24%), m.p. 193—195 °C, which has already been isolated as an intermediate in the preparation of erysotrine (**1**).[3] A similar treatment of (**16**) gave an isomeric dehydro-compound (**18**).

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