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STRUCTURE REVISION OF "1-KETO-α-CYPERONE," A SESQUITERPENE ISOLATED FROM TOBACCO[1)]

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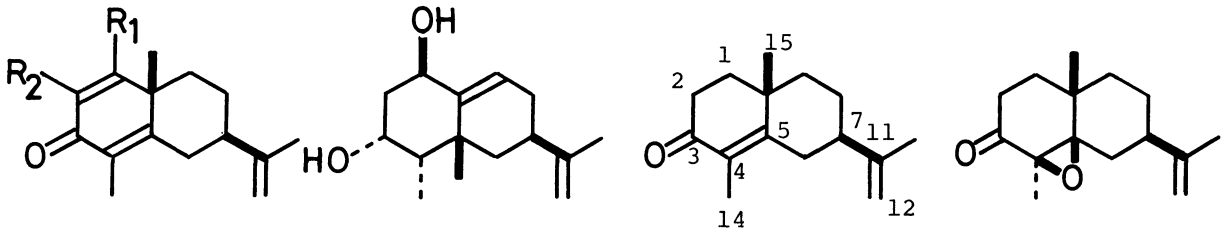
The structure of "1-keto-α-cyperone" isolated from tobacco was revised to 2-keto-α-cyperone on the basis of the unambiguous transformation of (+)-α-cyperone into the compound.

The title compound (1), "1-keto-α-cyperone," a sesquiterpene isolated from burley and flue-cured tobacco (Nicotiana tabacum), was assigned formula 1' by Roberts.[2)] On account of the C-1 oxygenated eudesmane structure, the compound was regarded as an intermediate relevant to a biogenetic pathway[3)] to capsidiol[4)] (2), one of the representative phytoalexins of the Solanaceae. However, in continuing biosynthetic studies on stress metabolites of the Family,[5)] we had some doubts about the proposed structure.[6)] In this paper we report that the structure (1') should be revised to 2-keto-α-cyperone (1) on the basis of the chemical transformation of (+)-α-cyperone[7)] (3) into 1, excluding the aforementioned biogenetic route.

The transformation of 3 into 2-keto-α-cyperone was performed straightforward as described below. Treatment of 3 with lithium diisopropylamide (LDA, 1.5 equiv) in tetrahydrofuran (THF) and then with molybdenum peroxide MoO_5·Py·HMPA (MoOPH, 1.5 equiv) (-78 °C, 1 h and room temp, 0.5 h)[8)] followed by further oxidation with manganese(IV) oxide in THF (room temp, 2.5 h) gave 2-keto-α-cyperone,[9)] mp 78-79 °C (from hexane), $[\alpha]_D^{20}$ -159.7° ($CHCl_3$), in 70% yield, which showed the following spectra; MS, m/e 232 (M^+) and 189 (base); UV (EtOH), λ_{max} 259.5 nm (ε 18000); IR (KBr), ν_{max} 3320, 1682 (small), 1625, 1331, 1311, 1280, 1231, 1187, 1162, 1054, 1020, 908, 878, and 792 cm^{-1}; NMR ($CDCl_3$), δ 1.26, 1.80, and 1.98 (each 3H, s, 15-, 13-, and 14-H), 4.80 (2H, s, 12-H), 6.03 (1H, s, 1-H), and 6.41 (1H, s, OH). These data were essentially identical with those[2)] reported for the compound (1), indicating that the relevant sesquiterpene is represented correctly by formula 1.

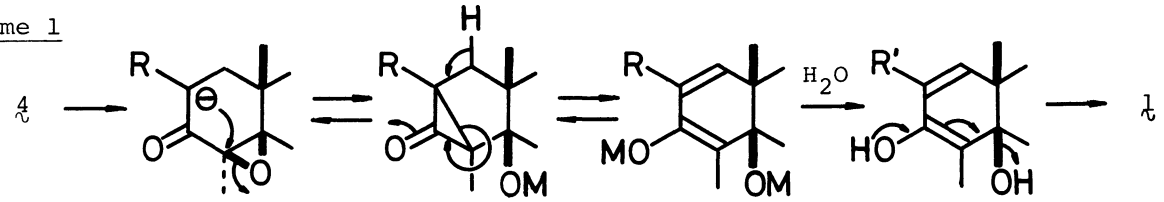
In connection with this, we describe alternate routes resulting in formation of the compound (1), which are rather lengthy but offer mechanistically intrinsic interest. (+)-α-Cyperone (3) was converted into the 4β,5β-epoxide[10)] (4) in 70% overall yield by a modification of the known procedure.[10)] Treatment of 4 with LDA (2 equiv) in THF and then with diphenyl disulfide (-78 °C, 1 h and room temp, 1 h)[11)] afforded 2-phenylthio-1,2-dehydro-α-cyperone (5), oil, $[\alpha]_D^{20}$ -98.2° ($CHCl_3$), which underwent hydrolysis with mercury(II) chloride (3 equiv) in 80% aqueous acetonitrile (reflux, 1 h)[12)] to give 1, mp 74-76 °C, $[\alpha]_D^{20}$ -171.0° ($CHCl_3$), in 30% overall yield. Alternately, epoxide 4, when treated with LDA (1.5 equiv) in THF and then with MoOPH (1.5 equiv) (-78 °C, 1 h and room temp, 0.5 h),[8)] was

converted into 1, mp 76-77 °C, $[\alpha]_D^{20}$ -166.4° ($CHCl_3$), in 73% yield. The novel reactions would be rationalized as shown in Scheme 1.[13]



1 R_1=H, R_2=OH
1' R_1=OH, R_2=H
5 R_1=H, R_2=SPh

Scheme 1



R=$OMoO_4L_2^-$ or SPh
M=Li
R'=OH or SPh

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