

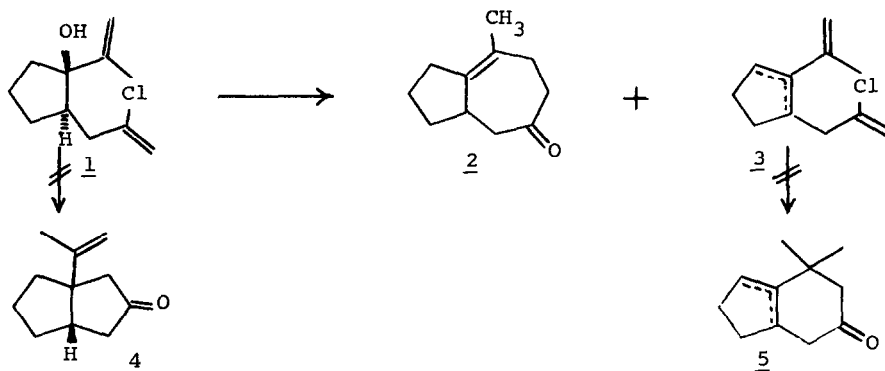
A DIRECT SYNTHESIS OF HYDROAZULENONES

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Of the various possible synthetic approaches to sesquiterpenes of the hydroazulene variety¹, solvolytic skeletal rearrangement of decalyl^{2,3} and bicyclo-(4,3,1)decanyl¹ tosylates has received the greatest amount of attention for preparing bulnesol and its guaiazulenic relatives. Although quite lengthy, these routes have allowed for partial^{1,3} or total² stereochemical control in elaborating the asymmetric centers in the precursors and hence also in the rearranged product. We now wish to report an extremely rapid construction of hydroazulenones wherein chloro olefin annelation⁴ permits direct entry into the bicyclo(5,3,0)decane ring system and, in addition, to a variety of 4- and/or 5-substituted azulenes.

Addition of 2-(2-chloroallyl)cyclopentanone⁵ to 2-propenylmagnesium bromide in tetrahydrofuran affords oily carbinol 1⁶ in ca. 80% yields. Formolysis of 1 (30 min at 70°), with continuous nitrogen flushing to remove HCl, followed by conventional hydrolysis and workup provides⁷ ca. 80% of ketone 2 (2,4-DNPH, mp 156-7°; reported⁸, mp 156-157°) whose spectral properties⁶ agree with those reported⁸. Additional confirmation of structure 2 comes from aluminohydride reduction and dehydrogenation with palladium-on-carbon in refluxing triglyme to provide 4-methylazulene⁹. Approximately 15% of uncyclized diene 3 (λ_{\max} 240 nm) accompanies ketone 2. It is noteworthy that other cyclic ketones such as 4 and 5, which could arise from 1 and 3, respectively, are not present in amounts readily detectable by careful ir and nmr analysis. Similar results are obtained with the



carbinol derived from vinyl-magnesium bromide addition to 2-(2-chloroallyl)cyclopentanone (leading to 2 with CH₃ replaced by H).

Once the problem of stereoselective introduction of the isopropyl side chain is solved and with the proper cyclopentanone in hand, model transformation 1 → 2 promises to become a preferred route for synthesis of many guaiazulenic sesquiterpenes. We shall report on these matters in detail at a later date.

References

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6. Characterized by an appropriate combination of ir, uv, nmr and mass spectrometry.
7. Vpc analyses were performed on a six foot Carbowax on chromosorb W column heated at 200°C and a helium flow rate of ca. 60 cc/min.
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