

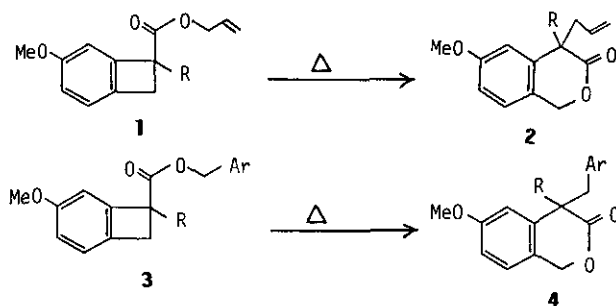
SYNTHESIS OF 4,4-DISUBSTITUTED ISOCHROMAN-3-ONE BY A TANDEM
ELECTROCYCLIC-SIGMATROPIC REACTION AND ITS APPLICATION TO
THE SYNTHESIS OF NATURAL PRODUCTS

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The development of a novel and practically useful tandem electrocyclic-sigma-
tropic reaction of benzocyclobutenes was accomplished. The thermolysis of 1-alkyl-
1-carballyloxybenzocyclobutenes (1), readily derivable from 1-cyanobenzocyclo-
butene, gave 4-alkyl-4-allylisochroman-3-ones (2) via a tandem electrocyclic-
[3,3]sigmatropic reaction in an excellent yield. On the other hand, 1-alkyl-1-
carbobenzyloxybenzocyclobutenes (3) afforded 4-alkyl-4-benzylisochroman-3-ones (4)
via a tandem electrocyclic-[1,3]sigmatropic reaction.



As an application of the methodology thus developed, a total synthesis of (±)-
physovenine (7), a minor alkaloid of Calabar bean, was successfully accomplished.
4-Allyl-6-methoxy-4-methylisochroman-3-one (6), obtained quantitatively from the
thermolysis of 5-methoxy-1-methylbenzocyclobutene (5) was converted to physovenine
in a 13-step sequence in 20 % overall yield. The procedure might be applicable for
synthesizing other alkaloids of Calabar bean.

