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A REVERSIBLE CLAISEN REARRANGEMENT OF 3-(3,3-DIMETHYLALLYL)-4-(3,3-DIMETHYLALLYLOXY)QUINOLIN-2-ONE; SYNTHESIS OF BUCHAPSINE AND LOSS OF ITS 1,1-DIMETHYLALLYL GROUP

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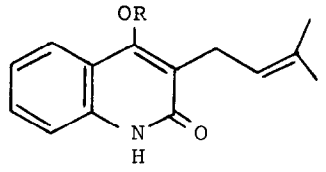
Summary. Reversible Claisen rearrangement of 3-(3,3-dimethylallyl)-4-(3,3-dimethylallyloxy)quinolin-2-one (5) furnished the alkaloid, buchapsine (6), which readily lost the 1,1-dimethylallyl group; a mechanism for the cleavage reaction is proposed.

Quinoline alkaloids have been isolated from many Haplophyllum species, especially by Yunusov and co-workers, but H. bucharicum was shown to produce an unusual group of monoterpenoid alkaloids apparently related through Claisen and abnormal Claisen rearrangement of geranyloxyquinolinone derivatives.[1] Two hemiterpenoid quinoline alkaloids, the C, O-diprenylquinolinone (5) and its Claisen rearrangement product, buchapsine (6) recently were identified as constituents of H. bucharicum[2] and we now report a study of the synthesis and interconversion of these alkaloids.

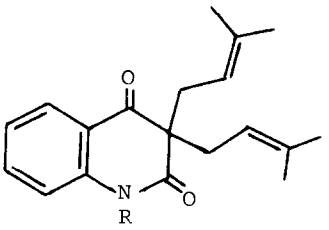
3-(3,3-Dimethylallyl)-4-(3,3-dimethylallyloxy)-quinolin-2-one (5) was isolated first from Haplophyllum tuberculatum[3] and was obtained by Reisch and co-workers[4] as one of six products of the allylation of 4-hydroxyquinolin-2-one. We prepared alkaloid (5) (10% yield) from 3-(3,3-dimethylallyl)-4-hydroxyquinolin-2-one (1) ($Me_2C{=}CHCH_2Br$, K_2CO_3, Me_2CO, reflux). The major product of this reaction was the bis-(3,3-dimethylallyl)derivative (3), and two minor constituents were shown by ^{1}H-n.m.r. spectroscopy and by their mass spectra to be the novel triprenyl derivatives (4) and (7).

When the O-prenylquinolin-2-one (5) was refluxed for 3 hours in N-methylpiperidine (b.p. 106°C), the Claisen rearrangement product (±)-buchapsine (6), m.p. 126°C was isolated and gave similar ^{1}H-n.m.r. and mass spectra to those recorded for the alkaloid; its structure was confirmed by ^{13}C-n.m.r. spectroscopy. Although the alkaloid is not reported to be optically-active, its higher melting point (134-135°C) suggests that it was obtained as an enantiomer. Separation of the products of the reaction by preparative t.l.c. furnished buchapsine (43%) and the starting C-, O-diprenylquinolinone (47%); since recovery of the latter was not altered significantly by prolonged reflux in N-methylpiperidine, it appeared that a reversible rearrangement took place. This was confirmed by submitting buchapsine (6) to the same reaction conditions when partial conversion into the C, O-diprenyl derivative (5) (47%) was observed. A minor product (6%) of the forward reaction was the 4-hydroxy-3-prenylquinolin-2-one (1) and this was obtained in higher yield (20%) in the reverse reaction. Assuming that the mono-prenyl derivative (1) is formed by loss of the 1,1-dimethylallyl group from buchapsine, it seems that the composition of the equilibrium mixture of compound (5) and buchapsine (6) is approximately 1:1. The same equilibrium [approximate composition 1:3 for compounds (5) and (6)] was also established by heating either compound with acetic anhydride and sodium acetate at 100°C for 3 hours; in these cases, the mono-prenyl product was trapped as its acetate (2) (46% yield in the forward reaction and 66% in the reverse reaction).

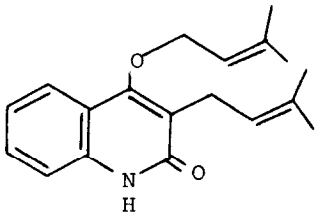
We attribute reversibility of the rearrangement to steric crowding at the C-3 quaternary carbon atom of buchapsine, as in the retro-Claisen rearrangement of 2-(1,1-dimethylallyl)-2-methylcyclohexanones.[5] The driving force for cleavage of the 1,1-dimethylallyl group of buchapsine may be aromatisation of the heterocyclic system with loss of isoprene, cf. (8), but clarification of the mechanism must await identification of the five-carbon fragment. The importance of the presence of the 1,1-dimethylallyl group of buchapsine for the rearrangement reaction and for loss of the allyl group is apparent from the stability of the bis-(3,3-dimethylallyl)quinolinone (3)



1 R = H
2 R = Ac



3 R = H
4 R = $CH_2CH{=}CMe_2$



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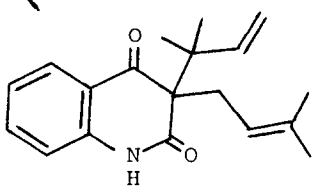

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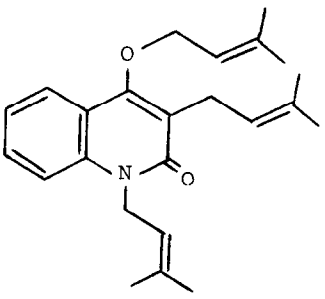

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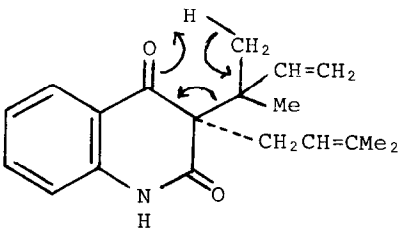

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when subjected to prolonged treatment with acetic anhydride and sodium acetate at 100°C.

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