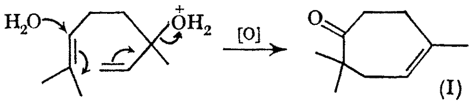
Synthesis of 2,2,5-Trimethylcyclohept-4-enone (Karahanaenone) *via* a New Terpene Cyclisation

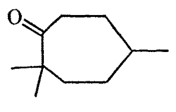
By E. DEMOLE* and P. ENGGIST

(*Research Laboratory, Firmenich et Cie.,* 1211 *Geneva* 8, *Switzerland*)

Summary Terpene alcohols such as linalool and nerolidol cyclise readily to the corresponding 2-alkyl-2,5-dimethylcyclohept-4-enones when brominated by *N*-bromosuccinimide and then heated under reflux in collidine.



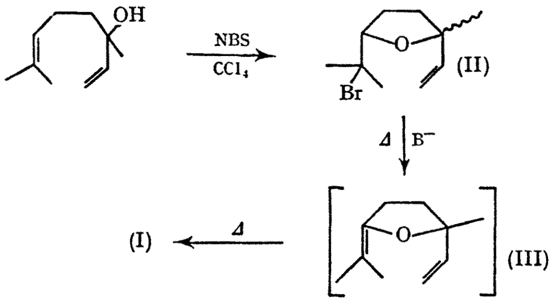
(I)



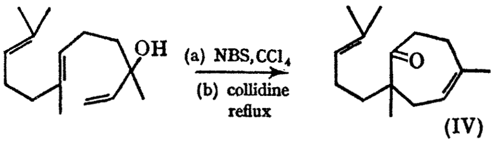
(Ia)

NAYA and KOTAKE[1] reported the isolation from hop oil of karahanaenone [2,2,5-trimethylcyclohept-4-enone (I)], and a synthesis of the related dihydro-ketone (Ia). We describe now the first synthesis of karahanaenone.

Although karahanaenone (I) could be derived from linalool by anti-Markownikoff cyclisation (Scheme), such a route is impracticable owing to the lack of general methods available for such cyclisations. However, in work on the bromination of alcohols with *N*-bromosuccinimide (NBS) we found that linalool behaves "abnormally" when brominated by NBS in CCl_4, at room temperature, and gives the α-bromotetrahydrofuran (II) as a major product. This in refluxing collidine, apparently undergoes dehydrobromination to an intermediate allylvinyl ether (III).†, which rearranges directly to karahanaenone (I) (overall yield of pure ketone, 62%). The i.r., n.m.r., and mass spectra of synthetic karahanaenone are identical with those of the natural ketone.‡



This reaction sequence can also be applied to, *e.g.*, nerolidol, which is smoothly converted into the cycloheptenone (IV) (65% overall yield), an attractive intermediate for the synthesis of bicyclic sesquiterpenes related to carotol.



Other examples of such bromination reactions involving the participation of a neighbouring hydroxy-group are known, for instance in the series of carotol[2] and of dammarane-type triterpenes,[3] although the synthetic possibilities of these reactions have not previously been considered.

In relation to the Claisen rearrangement of 5-isopropylidene-2-methyl-2-vinyltetrahydrofuran (III), it should be pointed out that Rhoads and Brandenburg[4]§ suggested a tetrahydrofuran derivative similar to (III) as one of the possible intermediates involved in the thermal rearrangement of 2,5-dimethyl-2-vinyl-2,3-dihydrofuran to 4-methyl cyclohept-4-enone.

We thank the Management of Firmenich et Cie, Geneva, and Dr. G. Ohloff, Research Director, for their kind support.

(*Received, January 20th, 1969; Com.* 078.)

† The hydrolysis product of (III), namely 6-hydroxy-2,6-dimethyloct-7-en-3-one is obtained in fair yield by heating (II) at 110° in collidine and treating the reaction mixture with dilute mineral acids.

‡ We thank Y. Naya and M. Kotake, Institute of Food Chemistry, Osaka, for the spectra of natural karahanaenone.

§ We thank Professor G. Büchi (M.I.T.) for bringing this to our attention.

[1] Y. Naya and M. Kotake, *Tetrahedron Letters*, 1968, 1645.
[2] J. Levisalles and H. Rudler, *Bull. Soc. chim. France*, 1967, 2059.
[3] O. Tanaka, N. Tanaka, T. Ohsawa, Y. Iitaka, and S. Shibata, *Tetrahedron Letters*, 1968, 4235; M. Nagai, N. Tanaka, S. Ichikawa, and O. Tanaka, *ibid.*, p. 4239.
[4] S. J. Rhoads and C. F. Brandenburg, *J. Amer. Chem. Soc.*, 1966, **88**, 4294.