

A NEW ROUTE TO STEREOSPECIFIC SYNTHESIS OF TERPENOID
1,5-POLYENES VIA ISOPRENE CYCLOOLIGOMERS

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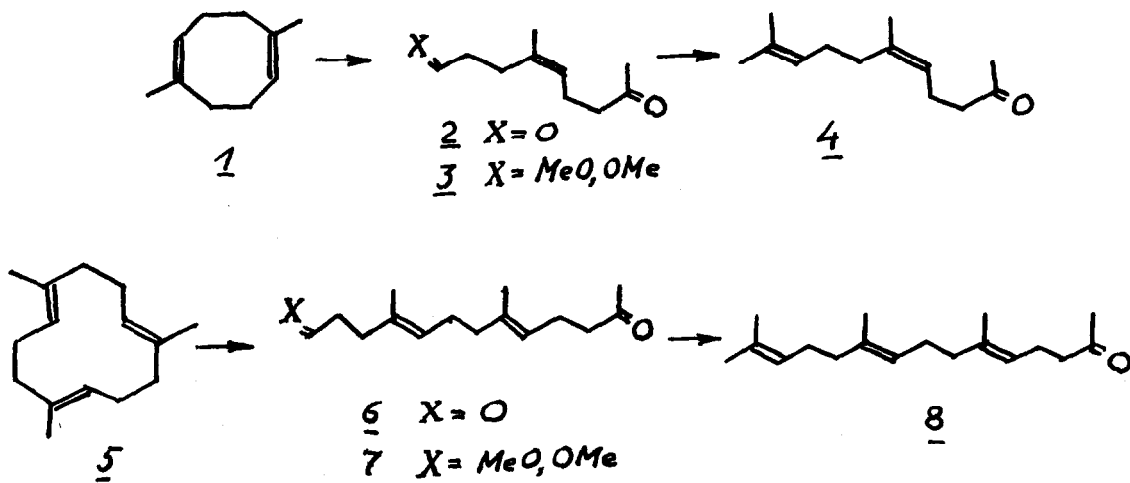
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The use of isoprene for construction of terpenoids is one of the most challenging problems of synthetic chemistry. Thermal¹ and catalytic^{2,3} isoprene oligo- and telomerization into terpenoids or related compounds is well documented in literature (mostly in patent form). This way, as a rule, allows one to obtain monoterpenoids, and for the synthesis of more complicated substances some preliminary functionalization of isoprene itself is needed⁴.

We wish to report here a new approach in utilization of isoprene for stereospecific synthesis of 1,5-polyenic terpenoids by means of the selective transformation of isoprene cyclooligomers with regular ("head-to-tail") structure. The approach is exemplified by transformation of available³ dimer 1 and trimer 2 into the corresponding keto aldehydes 2,6 and their dimethyl acetals 2,7 (Scheme). These compounds, which alternatively could be obtained by oxidative cleavage of the respective unsaturated ketones of type 4,8^{5,6} are widely used in the synthesis of various acyclic and cyclic isoprenoids.

The most natural way to desirable transformation of the isoprene cyclooligomers under consideration consists of their partial ozonolysis. Such ozonolysis is known for some polyolefins⁷, but compounds 1 and 2 are not involved, to our knowledge, in this reaction.⁸

Scheme

It was found that the interaction of 1 or 5 with 0.9 mol equiv. of O_3 in cyclohexane at ca. 10° in the presence of 2 mol equiv. of MeOH proceeds with a high selectivity (ca. 95%), leading to cleavage of only one C=C bond. Subsequent hydrogenation of insoluble monocozonides over a Lindlar catalyst gives, respectively, keto aldehydes 2 or 6 with a yield of about 50%.

The structure 2 was established by direct comparison (IR, NMR, VPC) with an authentic sample⁶ of Z-(2). Previously unknown E,E-(6) proved to be an oily substance with a b.p. $128^\circ/1$ mm Hg; IR (neat) ν : 1710, 1725 cm^{-1} ; NMR (CCl_4) δ : 1.40 (6H, $CH_3C=C$), 1.9–2.0 (12H, CH_2), 2.03 (3H, $CH_3C=O$), 4.65 (2H, $HC=C$), 9.59 ppm (1H, $HC=O$)⁹.

Both keto aldehydes react at -78° with 1 mol equiv. of $Ph_3P=CMe_2$ (generated by the action of n-BuLi on parent phosphonium bromide in THF-hexane solution) to give, in a yield of ca. 50%, the corresponding unsaturated ketones which are identical (IR, NMR, VPC) to samples of Z-geranyl-(4)¹⁰ and E,E-farnezyllactone (8)¹¹.

Thus the transformations mentioned above represent the three step stereospecific preparation of important synthons starting from isoprene, the last stage of the sequence being a new example of selective olefination of polycarbonyl compounds¹².

Keto aldehydes **2** and **6** were converted smoothly under standard conditions into the corresponding dimethyl acetals **3**⁹ [b.p. 42-43°/1 mm Hg; IR (neat) ν : 1720 cm^{-1} ; NMR (CCl_4) δ : 1.60 (3H, $\text{CH}_3\text{C}=\text{C}$), 1.98 (3H, $\text{CH}_3\text{C}=\text{O}$), 1.8 - 2.6 (8H, CH_2), 3.15 (6H, CH_3O), 4.20 (t, 1H, $J=5.0$ Hz, OCHO), 4.98 ppm (1H, $\text{HC}=\text{C}$)] and **7**⁹ [b.p. 127°/1 mm Hg; IR (neat) ν : 1715 cm^{-1} ; NMR (CCl_4) δ : 1.53 (6H, $\text{CH}_3\text{C}=\text{C}$), 1.96 (3H, $\text{CH}_3\text{C}=\text{O}$), 1.7 - 2.4 (12H, CH_2), 3.13 (6H, CH_3O), 4.16 (t, 1H, $J=4.5$ Hz, OCHO), 4.99 ppm (2H, $\text{HC}=\text{C}$)]. This selective protection of one C=O group in keto aldehydes **2,6** leads to an interesting possibility for employment of these substances in various chemical transformations, including the synthesis of polyprenols. Examination of the synthetic values of this outlined approach is in progress in these laboratories.

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