SYNTHESIS OF Z,Z-TRISHOMOFARNESAL TERT-BUTYLIMINE

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A highly stereoselective method was developed for the preparation of Z,Z-trishomo-
farnesal tert-butylimine, a key block synthone required for the construction of
polyisoprenols with a nonnatural configuration of the "head" end of the chain, us-
ing as a basis the controlled condensation of aldehydes with aldmines. It was
shown that introduction into the condensation of aldehydes containing an acetal
grouping at the ω-position results in the formation of considerable amounts of
aldols. The use of α-trimethylsilyl derivatives of aldmines makes it possible
to dispense with this process and to direct the reaction toward the desired E-
acroleins.

The use of the "block" scheme we have proposed for constructing linear isoprenoids [1],
as applied to fully cisoid analogs of polyisoprenols, for example to hexaprenol WC₆OH [2], re-
quired development of a reliable method of synthesis of the aldmine (I) indicated in the
heading. The limited availability of Z,Z-farnesol, an obvious precursor of (I), prompted
us to study the possibility of obtaining this block-synthone starting from the substantial-
ly more readily available nerol, using for the Z-C₅-propagation of the "tail" fragment of
its chain the glutaraldehyde monoacetal, similarly as tert-butylimine of this aldehyde was
used by us for the Z-C₅-elongation of the "head" end of the isoprene chain in the synthesis
of the above-mentioned hexaprenol [2]. The results thereby obtained are presented in the
present article.

The alkylation of neryl sulfide (II) with β-bromopropanal ethyleneacetal gives sulfide
(III), the reductive desulfuration of the latter gives acetal (IV), the hydrolytic split-
tting of this gives aldehyde (V), and finally, treatment of (V) with t-BuNH₂ gives aldmine
(VI) (Scheme 1). The cross-combination of (VI), deprotonated by means of lithium diiso-
propylamide (LDA), with glutaraldehyde monoacetal (VII) [2] gives a mixture of the expected
E-acrolein (VIII) in a good yield with an approximately fivefold amount of much more polar
product which is readily separated by chromatography. The presence of absorption bands of
the OH (3600 cm⁻¹) and CHO groups (1720 cm⁻¹) in the latter's IR spectrum, conforms well
with the structure of aldol (IX). Confirming this structure, there are in the ¹H and ¹³C
NMR spectra of this compound the CHO signals in particular at δ ~ 9.7 and 205 ppm, respec-
tively, doubled because of diastereomerism, together with signals at 2.4 and 55 ppm, cor-
responding to the HCCOCHO fragment.
Attempts were unsuccessful to convert aldol (IX) into a disubstituted acrolein (VIII) under the conditions (pH ≥ 4, -20°C) to ensure the later retention of the acetal protecting group required in subsequent operations. Therefore, aldehyde (VII) was subjected to olefinization according to Peterson, which made it possible to avoid (cf. [3]) the formation of ballast products of type (IX). The trimethylsilyl (TMS) component required for this, which is readily obtained by treating aldimine (VI), deprotonated by means of LDA, with Me₃SiCl, was found to be fairly unstable, and was used subsequently without isolation. The controlled cross-combination of TMS-(VI) with (VII) under the previously found conditions [1] gave a mixture of acroleins (VIII) in an overall yield of 45%, in a ratio of E/Z ~ 5:1, as found by comparison in the PMR spectrum of the total product of the integral intensities of the singlet CHO signals for the main (δ ~ 9.3 ppm) and admixed (δ ~ 10 ppm) stereoisomers, cf. [1, 4]. The content of the undesired, thermodynamically less suitable Z-isomer (cf. [5]) could be reduced to ~3% (PMR) by holding the obtained sample of (VIII) in a CHCl₃ solution (AR) at -20°C for a week, or for 6 h at 140-150°C in a sealed ampul.

The E-acrolein (VIII) which was found to be on the whole preparatively available was further stereospecifically transformed without any difficulties (cf. [1, 2]) into the Z,Z-trishomofarnesal (XII), and then into the desired aldimine (I), via the intermediate stages of allyl alcohol (X), its O-sulfate (not isolated) and acetal (XI) in an overall yield of ~10% in the nine above-discussed stages (Scheme 1). The structure of the previously unknown compounds was confirmed spectrally.