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# C-PRENYLATION OF ISOPENTENYL DERIVATIVES WITH SULFONIUM SALTS

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Abstract :
Reaction of isopentenyl acetate (or n-butyl ether) with oil soluble prenyl sulfonium salts in the presence of a hindered amine leads to prenylation on the terminal carbon atom.

Following up on previous studies on the biomimetic synthesis of isoprenoids by acid promoted prenylation of various olefinic substrates[1], we decided to investigate the prenylation of isopentenyl derivatives 1 with the now readily available[2] prenyl sulfonium salts 2.

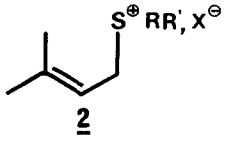
Little work has been done on the alkylation of non activated olefins with sulfonium salts. This is of considerable interest in connection with the enzymatic methyl transfer using S-adenosyl methionine as methyl donor[3]. The only example reported[4] is the intramolecular cyclisation of a cycloheptenylmethyl dimethyl sulfonium salt on heating in water in the presence of calcium carbonate at 100-150°.

Isopentenyl methyl prenyl sulfonium methane sulfonate 3, R=Me, $X=MeSO_3$ was readily formed (100%) from isopentenyl methyl sulfide[5] and dimethyl vinyl carbinol (2 eq.) in methane sulfonic acid (4 eq., r.t., 3 days in $CH_2Cl_2$)[6]. Anion exchange with perchloric acid in aqueous methanol gave the corresponding perchlorate 3, R=Me, $X=ClO_4$, 100%.

A concerted rearrangement of this salt is forbidden[7] but bond fission might generate a prenyl "cation" in the neighbourhood of the isopentenyl derivative. The corresponding ether is known to undergo such a conversion catalysed by Lewis acids[8a] or a proton[8b].

Heating 3, R=Me, $X=ClO_4$ at 60° in $CDCl_3$ in an NMR tube led to its disappearance (completion in one hour) to give first diprenyl methyl sulfonium perchlorate, and then black tars. The presence of a base was therefore necessary. Calcium carbonate[4] was ineffective in preventing this, probably

due to its insolubility. Triethylamine was converted at 60° to prenyl triethyl ammonium perchlorate which further decomposed to isoprene. We finally chose diisopropylethylamine (Hünig's base) which dissolved the salt and proved to be sufficiently hindered not to be prenylated.

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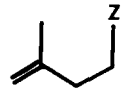


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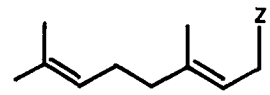


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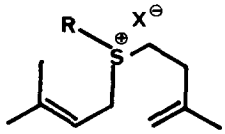


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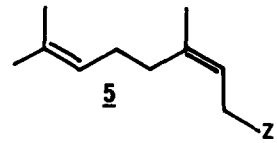


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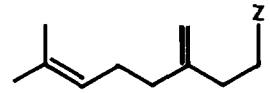


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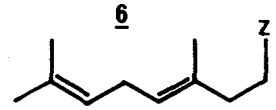


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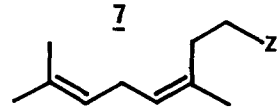


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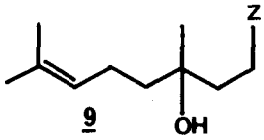


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On heating with Hünig's base (3 eq.) at 70°C the salt 3, R=Me, X=$ClO_4$, disappeared within 20 h and the amine perchlorate separated. GLC analysis showed that a mixture of olefins 4 - 8, Z=SMe had been formed in ca 20% yield together with some diprenylated compounds. Authentic samples were secured by dehydration ($POCl_3$, pyridine) of alcohol sulfide 9, Z=SMe[9].

The counter ion of the sulfonium salt is of critical importance : the salt 3, R=Me, X=$CH_3SO_3$ gave prenyl methane sulfonate. The aromatic sulfonium salt 3, R=Ph, X=$ClO_4$ decomposed rapidly at room temperature to isoprene and the corresponding sulfide and dit not, so far, give any prenylation products.

The non concerted character of the above prenylation and the formation of diprenylated products encouraged us to try an intermolecular reaction. Heating dimethyl prenyl sulfonium perchlorate 2, R=R'=Me, X=$ClO_4$ with Hünig's base and 1 (Z=OAc) at 60° did not lead to prenylated products, perhaps due to the poor solubility of the salt. We therefore used the corresponding didodecyl salt 2, R=R'=$C_{12}H_{25}$ [10] which gave a homogeneous solution with Hünig's base (2 eq.) and isopentenyl acetate 1, Z=OAc (3 eq.). Heating this mixture at 70° resulted in complete decomposition of the salt within 20 h and precipitation of the amine salt. A mixture of olefins 4 (10%), 6 (19%), 7 (47%) and 8 (24%), Z=OAc was isolated by chromatography on silica gel (total yield) 24%). The composition of the mixture was determined by capillary GLC and by comparison with authentic samples[8b]. Using a larger excess (10 eq.) of 1, Z=OAc led to a slightly better yield (33%). With the more hindered 2,6-di-t-butyl pyridine and Z=OAc (3 eq.) a 21% yield was obtained. Hünig's base and tetrafluoroborate as the counter ion gave 33% yield. Isoprene was also formed together with didodecyl sulfide.

With isopentenyl n-butyl ether 1, Z=O-n-Bu (3 eq.), the perchlorate salt (1 eq.) and Hünig's base (2 eq.) gave a 35% yield of olefins 6 (22%), 7 (53%) and 8 (25%), Z=O-n-Bu.

It thus appeared possible to achieve the prenylation of isopentenyl derivatives with prenyl sulfonium salts. This encouraged us to investigate the biomimetic methylation of olefins. The results will be published shortly[11].

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