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An Unusual Selectivity Change in the Acetylation of 1,8-Dihydroxy-3,7-dimethyl-9-(2′,6′6′-trimethylcyclohexen-1′-yl)nona-2,4,6-triene under Phase-transfer Catalysis

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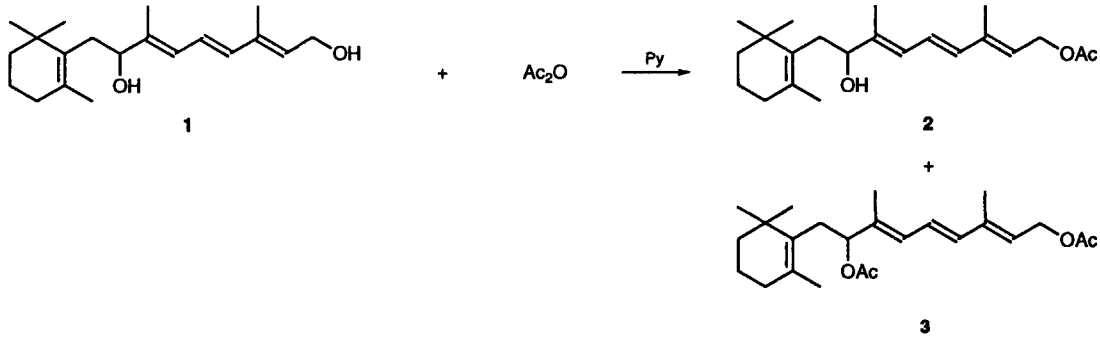
During acetylation of an intermediate in vitamin A synthesis under phase-transfer catalysis in the solid-liquid system, only monosubstitution occurs in contrast to acetylation in the homogeneous system.



One of the stages of vitamin A synthesis by the method of Preobrazhensky and Samokhvalov is the acetylation of 1,8-dihydroxy-3,7-dimethyl-9-(2′,6′,6′-trimethylcyclohexen-1′-yl)-nona-2,4,6-triene **1** with acetic anhydride.[1]

Usually the ratio of products of di- and monoacetylation in this reaction is **3**:**2** = 4:1. However, this method has certain disadvantages, such as the use of a toxic reagent, pyridine, as a catalyst. The method of solid-liquid phase-transfer catalysis (PTC) has been widely used in the last few years.[2] We have studied the possibility of acetylation of compound **1** in such a system. As a solid base Na_2CO_3, K_2CO_3, $NaHCO_3$, NaOH, KOH and $CaCO_3$ were used. A commercially-available quaternary ammonium salt dimethylbenzylalkyl (C_{12}–C_{16}) ammonium chloride was used as a catalyst, and methylene dichloride or hexane as solvents. In a typical run 150 ml of hexane, 11 g of **1**, 5–8 g of solid base and 0.8 g of the catalyst were placed in a reactor and 0.004–0.008 ml of acetic anhydride was added over 30 min at 28–35 °C and the mixture was stirred for 3–4 h. The reaction mixture was analysed by HPLC (eluent, 3% Pr^iOH in hexane; column, Silasorb C 600; wavelength, 230 nm).

Acetylation of **1** under PTC conditions proceeds nearly quantitatively just as with pyridine, but the ratio of products **2** and **3** changes drastically. The dominant product with any solid

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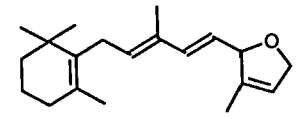
Table 1 Acetylation of **1** in hexane in the presence of different solid bases (28–35 °C, reaction time 1 h, **1**:Ac_2O = 1:2).

Base	Ratio **2**:**3**
Pyridine[a]	1:4
Na_2CO_3	100:1
$NaHCO_3$	100:1
K_2CO_3	100:1
NaOH[b]	100:1
KOH[b]	100:1
$CaCO_3$[c]	100:1

[a] Without the catalyst. [b] A significant quantity of side-product was obtained. [c] The reaction proceeds extremely slowly; even after 8 h the degree of conversion is only *ca.* 50–60%.

base is the monoacetylated diol **2**. The case of $CaCO_3$ is the exception. Traces of **3** appear only when conversion of **1** exceeds 75%. The results obtained are summarized in Table 1.

It must be mentioned that when the reaction is carried out in the presence of NaOH and especially KOH a number of side-processes occur. In order to isolate and identify their products we have performed some runs in conditions favourable to their formation (solid KOH, 40 °C). The fractions of reaction mixture containing these compounds were obtained with the help of preparative HPLC (sorbent, silica gel L, 20–40 mm; eluent, hexane – Pr^iOH, 10:1). We then obtained some viscous, tarry products with total yield not more than 5–7%. Based on some spectroscopic data (IR, ^1H NMR and mass spectroscopy[‡]) to these products was tentatively assigned the general structure **4** (including various stereoisomers). Also obtained was a dimeric product with molecular mass 572.



4

In our opinion the secondary hydroxy group of the diol **1** is much more hindered than the primary one, due to diol adsorption on the surface of the solid base; this may explain the observed reaction selectivity. A weaker base, such as $CaCO_3$, is not able to adsorb diol **1** as strongly as Na_2CO_3 or stronger bases, so the selectivity of the reaction in its presence is the same as in a homogeneous reaction.

[‡] Absorption bands at 1085 cm^{-1}, chemical shift at 3.5–3.2 ppm.

References

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