# The Regiospecific Formation of $^{13}$C-Labelled Benzoins

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*Summary* Specifically $^{13}$C-labelled benzoins have been prepared by the *O*-(trimethylsilyl)cyanohydrin method in a completely regiospecific manner and shown to be extremely sensitive to scrambling, thus establishing this acyl-anion equivalent as the best one for labile products.

α-Hydroxyketones (acyloins and benzoins) are an important class of compounds with a long history of use in organic chemistry.[1,2] If the hydroxy-group is secondary, equilibration is possible through the intermediacy of an enediol (or the corresponding anionic forms). Thus a binary mixture often results,[3] although differences in thermodynamic stability can favour one product to the exclusion of the other.† This communication concerns the first preparation of specifically $^{13}$C-labelled benzoins of high isomeric purity by a method[4] which, in the light of the results presented below, should prove useful for easily isomerized benzoins and other labile α-hydroxyketones as well.

Treatment of a tetrahydrofuran (THF) suspension of the lithium carbanion of benzaldehyde *O*-(trimethylsilyl)-cyanohydrin (1·0 mmol, generated at −70 °C using 1·0 equiv. lithium di-isopropylamide) with [1-$^{13}$C]benzaldehyde (1·0 mmol, 0·1 mol $l^{-1}$) resulted in a homogeneous yellow solution. Warming to −15 °C (internal thermometer) caused the solution to cloud as LiCN precipitated.‡ After coming to room temperature (1 h) the mixture was quenched with 80% acetic acid and stirred for 20 h to hydrolyse the benzoin trimethylsilyl ether.§ The labelled benzoin (**1**) was isolated in 93% overall yield after partitioning the reaction mixture between water (pH 6) and dichloromethane, followed by chromatography of the organic residue on silica gel. Examination of this material by $^{1}$H n.m.r. and $^{13}$C n.m.r. revealed that $<2\%$ of the label was present in the carbonyl-group.¶ Repeating the synthetic sequence with labelled *O*-(trimethylsilyl)cyanohydrin and ordinary benzaldehyde gave material in which all the detectable label was present at the carbonyl-carbon atom.

An otherwise symmetric compound such as this is ideal for studying the enediol rearrangement because of the absence of thermodynamic effects favouring either possible isomer. The labelled benzoin is very sensitive to both base and heat. For example, stirring the original reaction mixture for 2 rather than 1 h gave material in which 5% of the label had been lost to the other position. Recrystallization of this material from reagent-grade ethyl acetate (boiled for $<1$ min) resulted in a further 5% transfer of the label [*i.e.* to give (**2**)].

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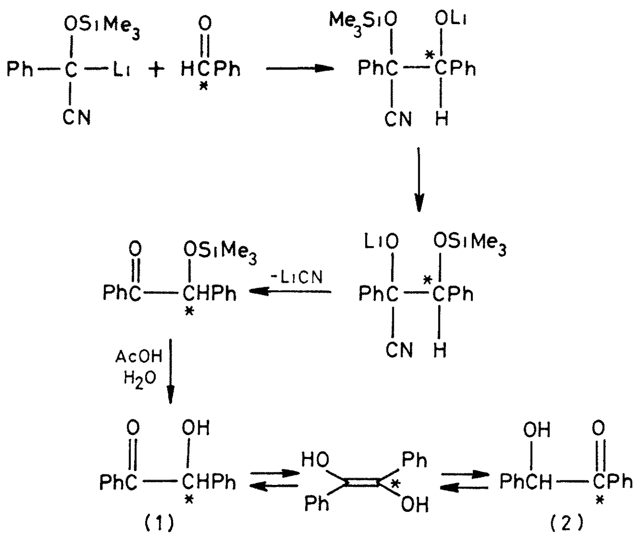
† According to ref. 2 (p. 277), 'In a benzoin condensation the carbinol-group never appears next to the 4-dimethylamino-substituted ring.'

‡ Identity confirmed by atomic absorption (Li) and three chemical tests for CN.

§ This product was isolated in 69% yield (recrystallized) using unlabelled benzaldehyde and proved identical to an authentic sample prepared from benzoin. The intermediate crude siloxyketone was characterized only spectroscopically in ref. 5.

¶ This represents an upper limit based upon uncertainties in measurement, since none of the carbonyl-labelled isomer could be detected above natural abundance.



In retrospect, it is clear that other acyl-anion equivalents such as the dithians[5] or differently protected cyanohydrins[6] would not have been satisfactory due to the more vigorous conditions required for their deprotection The *O*-(trimethylsilyl)cyanohydrin derivative was chosen in anticipation of this sensitivity, since it has been reported that optically active benzoin is rapidly racemized by catalytic base [7] The 1,4-rearrangement of the trimethylsilyl-group transforms the deprotection problem from that of unmasking a cyanohydrin (for which base treatment is necessary) to that of unmasking a silyl ether, which may be accomplished by a mild acid Optically active benzoin is racemized only slowly by acid at room temperature [8]

Since α-siloxyketones have been converted into silyl enol ethers,[9] this demonstration that they can be prepared in a highly regiospecific manner should spark keen interest in this class of compounds, which otherwise have only been prepared by the oxidation of silyl enol ethers[10] or by way of acyloin condensation products [11] The labelled benzoins themselves should prove valuable for the study of photochemical reaction mechanisms and other physical-organic studies

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