Ion Pair Extraction in Preparative Organic Chemistry

VI. Alkylation of Acetylacetone

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The alkylation of acetylacetone presents an interesting preparative problem. The anion of acetylacetone is a rather weak nucleophile and acetylacetone is alkylated much slower than ethyl acetacetate and diethyl malonate. In a protic solvent the reaction is usually too slow to give an acceptable reaction time. In an aprotic solvent such as DMSO the rate is acceptable, but the main product is now the O-alkylated product.1 In some recent publications it has been demonstrated that O-alkylation also occurs to some extent under other conditions.2 The best compromise to date is to use acetone as a solvent and K₂CO₃ as the base, although the reaction time is still very long (20 hours for methylation).3 The time can be considerably decreased using Rb₂CO₃ or Cs₂CO₃ as the base,4 but these are too expensive for routine use. The tetrabutylammonium ion behaves like a large alkali ion in many reactions. It can be expected therefore, that the tetrabutylammonium salt of acetylacetone is very rapidly alkylated.

We have recently demonstrated that tetrabutylammonium salts are readily prepared by ion pair extraction,4 and that the salt of methyl cyanoacetate is rapidly alkylated in a chloroform solution.6 We have now applied the same method to acetylacetone. Even in the present case the reaction is very rapid and the alkyla-

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Table 1.

<table>
<thead>
<tr>
<th>Alkylation agent</th>
<th>R</th>
<th>R</th>
<th>OR</th>
<th>Reaction time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl iodide</td>
<td>CH₂COCCH₂C</td>
<td>CH₂COCCH₂C</td>
<td>CH₂C=CHCOC</td>
<td>1.5</td>
</tr>
<tr>
<td>Ethyl iodide</td>
<td>72</td>
<td>16</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Isopropyl iodide</td>
<td>50.5</td>
<td></td>
<td>49.5</td>
<td>30</td>
</tr>
<tr>
<td>Butyl iodide</td>
<td>87</td>
<td></td>
<td>13</td>
<td>15</td>
</tr>
</tbody>
</table>

* The conventional procedure in methylation of acetylacetone is reported to yield a product containing about 10% of 3,3-dimethylpentane-2,4-dione. We did not succeed in separating the methylated products by gas chromatography. The elution of the products made the NMR-spectrum very complicated. The figure in Table 1 therefore is the sum of mono- and dimethylated products.

Hydride in the presence of boron trifluoride. This gives a product free from α-alkylated compounds but which contains small quantities of the isomers 2,4-hexanediol or 2,4-heptane-dione. 3-Isopropylacetylacetone was synthesized according to the method described in Org. Syn., A product rich in 4-methoxyprop-3-en-2-one can be prepared in acceptable yields by alkylation of acetylacetone with dimethyl sulphate in DMG, analogously with the method described by Joffe. Dialkylated products were prepared by alkylation of the substances obtained from the work referred to above by the same method as that used for acetylacetone. The gas chromatographic analyses were carried out directly on the evaporated reaction mixture by means of a 2 m x 1/8” column packed with carbowax 20 M (5%) at 160°C, with 40 ml/min N₂ flow.

**Experimental. Tetraphenylammonium salt of acetylacetone.** 0.5 Mole (170 g) of tetrabutylammonium hydrogen sulphate was added to a cooled solution of 1.1 mole of sodium hydroxide in 500 ml of water. 0.5 Mole (50 g) of acetylacetone was added and the solution was extracted with 500 ml of chloroform. The chloroform layer was evaporated and the crystalline residue was recrystallized from acetone. The yield of the salt was 70% and the melting point 155°C.

**Alkylation procedure.** The double excess of alkyl iodide was added to a stirred solution of the tetrabutylammonium salt of acetylacetone in chloroform as reported in the alkylation of methyl cyanoacetate. The chloroform and the excess of alkyl iodide were evaporated and the tetrabutylammonium iodide precipitated by adding ether to the residue. After filtration the ether was evaporated and the residue analysed as described above.

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