ACYLATION OF BENZIMIDAZOLE BY THE REGEL--BUECHEL METHOD.

2.* DEACYLATION AND DISSOCIATION OF 1-METHYL-3-ACYL-2-(1'-METHYL-2'-BENZIMIDAZOLYL)-4- BENZIMIDAZOLINES

B. I. Khristich and E. V. Bondarenko

With excess acyl halide 1-methyl-3-acyl-2-(1'-methyl-2'-benzimidazolyl)-4-benzimidazoline is converted to an unstable 1-methyl-3-acyl-2-(1'-methyl-3-acyl-4'-benzimidazolin-2'-yl)benzimidazolium chloride, which undergoes intramolecular redox cleavage with the formation of 1,1'-dimethyl-2,2'-dibenzimidazolyl and an aldehyde and dissociates at the C--C bond that connects the benzimidazolium and benzimidazoline fragments into a carbene yield and a 1-methyl-3-acylbenzimidazolium chloride.

It has been previously shown that the direct acylation of benzimidazole (Ia) [2] and 1-methylbenzimidazole (Ib) [1] in the 2 position by the action of aroyl halides via the Regel--Buechel method [3, 4] leads to the formation of chiefly coupling products II, which can be converted to 2-acyl-benzimidazoles III by heating with the corresponding acyl halides in acetonitrile in the presence of triethylamine [1].
TABLE 1. Deacylation of Bis Products IIb-d

<table>
<thead>
<tr>
<th>Compound</th>
<th>T&lt;sub&gt;mp&lt;/sub&gt; °C</th>
<th>Yield of IV, %</th>
<th>II isolated, %</th>
<th>Yield of IV, %</th>
<th>II isolated, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>170–171 [1]</td>
<td>.44</td>
<td>48</td>
<td>18</td>
<td>49</td>
</tr>
<tr>
<td>IIc</td>
<td>168–169 [1]</td>
<td>41</td>
<td>53</td>
<td>15</td>
<td>58</td>
</tr>
<tr>
<td>III&lt;sup&gt;*&lt;/sup&gt;</td>
<td>145–147</td>
<td>48</td>
<td>47</td>
<td>24</td>
<td>36</td>
</tr>
</tbody>
</table>

*This compound was crystallized from aqueous alcohol.

A priori this product could have been formed by thermal decomposition of II with the splitting out of an aldehyde. However, this assumption was not confirmed experimentally (acetonitrile, 100°C, 2 h); this indicated the decisive role of the acyl halide in this process. In fact, the addition of 1-2 moles of the acyl halide to a suspension of II in absolute benzene (toluene) led to the formation of IV when the reaction mixture was shaken for 2 days at 20°C (see Table 1).

In acetonitrile one observes a decrease in the yield of the deacylated product by a factor of more than two, and 1-methylbenzimidazole I is formed.

Regarding the acyl halide as an oxidizing agent, we attempted to replace it with nitrobenzene; however, we observed virtually no formation of deacylation product IV (70°C, 1 h, in solution in acetonitrile). This constitutes evidence that a decisive role in the deacylation of II is played by their prior coordination with the acyl halides, as a result of which V is formed. Its structure is confirmed by the corresponding absorption frequencies of the carbonyl group in the IR spectrum of a mixture of starting compound IIb and benzoyl chloride in a molar ratio of 1:2 in solution in chloroform: 1660 (CO group of the imidazoline fragment of V), 1740 (CO group attached to the imidazolium N heteroatom), 1790 cm<sup>-1</sup> (absorption of the carbonyl group of benzoyl chloride, which is present in excess amounts). The last two assignments were confirmed by the IR spectrum of a mixture of 1-methylbenzimidazole and benzoyl chloride at a molar ratio of 1:2.

We assume that the mechanism of the deacylation of intermediate V consists in hydride migration from the imidazoline fragment to the imidazolium carbonyl carbon atom with the formation of VI. The fact of the deacylation of IIb by the action of trifluoroacetic acid was unexpected. The transformation proceeds smoothly in ~80% yield at 20°C after 5-6 h.

Let us note that dilute mineral acids lead to the complex transformation of IIb to give a number of products, among which 1-methylbenzimidazole, 1-methyl-2-formylbenzimidazole, bis product IV, and unidentified compounds were detected.

The decrease in the yields of deacylated product IV on passing from benzene to acetonitrile and the variable formation in a solution of the latter of 1-methylbenzimidazole constitute evidence for dissociation of quaternary salt V at the C-C bond joining the benzimidazolium and benzimidazolone fragments into carbene yield VII and quaternary salt VIII. This assumption is also confirmed by the formation of 1,3-dimethylbenzimidazolium iodide in the reaction of IIb with methyl iodide both in acetonitrile and chloroform.

Let us note that both the hydride migration, which leads to deacylated product IV, and dissociation of quaternary salts V and IX are due to the same reason — the tendency of the imidazolone fragment of the molecule to undergo aromatization (which is accompanied by oxidation here) — and, consequently, are competitive processes. Decacylation is suppressed in polar solvents, which facilitate dissociation, whereas dissociation is suppressed in nonpolar solvents, and deacylation increases.

Taking into account the fact that quaternary salt V can be converted to 1-methyl-2-acetylbenzimidazole only when it dissociates (both as a consequence of intramolecular stabilization of carbene yield VII and by way of its reaction with the acyl halide), one can understand the decisive role of the polarity of the solvent and high temperatures (above 140°C) in its conversion to 2-acyl derivatives. The higher the temperature, the higher the rate at which carbene yield VII undergoes intramolecular conversion to the 2-acyl derivative and the smaller the likelihood of its conversion (via the reaction with quaternary salt VIII) to bis compound V and irreversible conversion of the latter to deacylated coupling product IV.