Formation of 2-Isoxazoline Derivatives and 3,5-Diarylisoaxozoles from 2,4,6-Triarylpivalium Salts. Norrish Type II Photoelminations
P. L. KUMLER, C. L. PEDERSEN and O. BUCHARDT

Chemical Laboratory II (General and Organic Chemistry), University of Copenhagen, The H. C. Ørsted Institute, Copenhagen, Denmark

The recent paper by Balaban 1 concerning the reaction of 2,4,6-triphenylpyrilylum perchlorate with hydroxylamine prompts us to report similar independent findings from our laboratory.

Balaban found that 2,4,6-triphenylpyrilylum perchlorate (Ia, X = ClO₄), when treated with hydroxylamine, gave the monoxime (IIa) of the pseudobase, which isomerized easily to the 2-isoxazoline IIIa. This isoxazoline was converted to the 3,5-diarylisoaxazole IVa and acetonaphone (Va) by treatment with 70% perchloric acid.

We have observed the same reaction sequence for a series of 2,4,6-triarylpivalium salts. Thus, reaction of the salts Ia-e (X = BF₄) with hydroxylamine in ethanol led to the formation of the corresponding 2-isoxazolines IIIa-e in good yield (see Table 1).*

The structures of the isoxazolines were assigned on the basis of elemental analyses and infrared, ultraviolet and NMR spectra (see Tables 1 and 2). The observed spectral properties are in excellent agreement with those reported by Balaban.1

In the previous work 1 conversion of the isoxazoline IIIa to the 3,5-diarylisoaxazole IVa and acetonaphone (Va) was brought about under strongly acidic conditions. We have found that this same transformation can be carried out under basic conditions or by photolysis. For example, refluxing the isoxazoline IIIa in alcoholic sodium hydroxide led to isolation of the isoxazole IVa in high yield (for other examples see the experimental section). The presence of acetonaphone (Va) in the reaction mixture was detected by NMR spectroscopy (see experimental). A reasonable mechanism for this transformation can be presented.

In the presence of base, the isoxazolines III are undoubtedly in equilibrium with two possible anions, VI and VI'. The equilibrium concentration of VI is expected to be smaller than that of VI', but elimination of the phenacyl substituent at C₄ as the enolate of acetonaphone, with concomitant formation of the stable isoxazole nucleus, is the driving force for the indicated sequence. The possibility that elimination of the phenacyl substituent takes place simultaneously with the removal of the C₄ proton cannot, however, be eliminated.

As additional support for the isoxazoline structure III, it was predicted that the...

*In some cases the monoxime was detected in the crude reaction mixture before recrystallization.
Table 1. Yields and physical properties of 2-isoxazolines IIIa-e.

<table>
<thead>
<tr>
<th>Compound</th>
<th>M.p.</th>
<th>% Yield</th>
<th>Formula</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>% C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Calc.</td>
</tr>
<tr>
<td>IIIa</td>
<td>123-124° C (A)</td>
<td>76</td>
<td>C_{13}H_{19}NO_{3}</td>
<td>80.91</td>
</tr>
<tr>
<td>IIIb</td>
<td>161-162° C (A)</td>
<td>48</td>
<td>C_{13}H_{19}NO_{3}</td>
<td>55.33</td>
</tr>
<tr>
<td>IIIc</td>
<td>102-104° C (B)</td>
<td>40</td>
<td>C_{13}H_{18}NO_{2}Cl</td>
<td>73.50</td>
</tr>
<tr>
<td>IIId</td>
<td>124-125° C (B)</td>
<td>35</td>
<td>C_{13}H_{18}NO_{2}</td>
<td>71.49</td>
</tr>
<tr>
<td>IIIe</td>
<td>124-128° C (B)</td>
<td>70</td>
<td>C_{13}H_{18}NO_{2}</td>
<td>78.17</td>
</tr>
</tbody>
</table>

*aRecrystallization solvent given in parentheses; A, benzene-hexane; B, ethanol. bRef. 1 gives m.p. 124°. cThis compound exhibits a double melting point with the lower m.p. 131-132° probably due to the isomeric form IIb. dNo attempt was made to maximize this yield.

Table 2. Spectral properties of 2-isoxazolines IIIa-e.

<table>
<thead>
<tr>
<th>Compound</th>
<th>IR</th>
<th>UV</th>
<th>NMR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C=O</td>
<td>λ_{max}</td>
<td>loge</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>IIIa</td>
<td>1690</td>
<td>254</td>
<td>4.36</td>
</tr>
<tr>
<td>IIIb</td>
<td>1670</td>
<td>263</td>
<td>4.63</td>
</tr>
<tr>
<td>IIIc</td>
<td>1680</td>
<td>253</td>
<td>4.45</td>
</tr>
<tr>
<td>IIId</td>
<td>1685</td>
<td>253</td>
<td>4.53</td>
</tr>
<tr>
<td>IIIe</td>
<td>1680</td>
<td>260</td>
<td>4.56</td>
</tr>
</tbody>
</table>

*aSpectra recorded in KBr. bSpectra recorded in 96% ethanol. c60 Mc/s, CDCl_{3} solution, Me_{4}Si internal reference; chemical shifts in τ values and coupling constants (J) in cps. dCalculated position of the A or B part of the AB quartet; H_{a}+H_{b} equivalent to two protons. eRelative intensity given in parentheses. fSpectra recorded in CHCl_{3}.

III \xrightarrow{hv} \begin{array}{c}
\text{Ar}^{1}\text{C-OH} \\
\text{H} \\
\text{Ar}^{2}
\end{array} \xrightarrow{\text{enolic form}} \begin{array}{c}
\text{Ar}^{1} \\
\text{CH}_{2} \\
\text{O} \\
\text{Ar}^{2}
\end{array} \xrightarrow{\text{IV} + \text{V}} \begin{array}{c}
\text{Ar}^{1} \\
\text{C} \\
\text{O} \\
\text{Ar}^{2}
\end{array}

Compounds should undergo the well-known Norrish "Type II" photolysis reaction of ketones possessing at least one γ-hydrogen atom. In agreement with this prediction, photolysis of the 2-isoxazolines IIIa-c and e (other solution, wavelength > 3000 Å) resulted in formation of the 3,5-diarylisoxazoles IVa-c, and e in good yield. The nitro-substituted 2-isoxazoline IIId, although photoactive, is not converted to the corresponding isoxazole IVd. We assume that the mechanism of the photoelimination involves abstraction of one of the γ-hydrogen atoms.

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the hydrogens at C_4 by an excited state of the ketone,* via a six-membered ring transition state, followed by cleavage to the enol form of the acetophenone derivative V and the 3,5-diarylisoxazole IV.

Experimental. Pyrylilum salts. These were prepared according to the method of Lombard and Stephan.  

Reaction of pyrylilum salts with hydroxylamine. This was performed (Table 1) analogously to the following procedure. 2,4,6-Triphenylpyrylilum fluoroborate (200 mg) was suspended in ethanol (10 ml). To the stirred suspension was added an aqueous solution of hydroxylamine hydrochloride (5 molar equivalents) and excess sodium hydroxide. The suspension was stirred for 18 h at room temperature. The 2-isoxazole IIIa (130 mg, 76%, m.p. 123—124°) was removed by filtration. This material was homogeneous by thin layer chromatography (TLC) and was recrystallized from benzene-hexane for analysis.

Preparation of 3,5-diarylisoxazoles (IV). a) Base-catalyzed method. A sample of 2-isoxazole IIIa (392 mg) was refluxed for 24 h in ethanol (200 ml) and aqueous 2 N sodium hydroxide (20 ml). The ethanol was removed on a rotary evaporator and 3,5-diphenylisoxazole (223 mg, 86%, homogeneous by TLC) was removed by filtration. Recrystallization from hexane gave colourless needles, m.p. 142.5—143° (lit. 4 m.p. 140—141°), identical (m.p., mixture m.p., infrared spectrum) with authentic samples of 3,5-diphenylisoxazole prepared from dibenzoylmethane and hydroxylamine.  

The filtrate above was extracted with CHCl_3, and the organic phase was dried over Na_2SO_4. The residue after evaporation of the solvent exhibited an NMR spectrum that indicated the presence of acetophenone (sharp singlet at 7.42  in CDCl_3).

By the above method, 3-(p-bromophenyl)-5-phenylisoxazole (IVb) was prepared in 67% yield (see physical properties below).

b) Photochemical method. A sample of 2-isoxazole IIIb (200 mg) was dissolved in 250 ml of ether in a Pyrex flask and photolyzed in a Rayonet reactor, type RPR-208, using the RUL-3500 lamps. After 38 h of irradiation the solvent was evaporated and the residue was separated by preparative layer chromatography on silica gel. In addition to an unidentified crystalline substance (21 mg) and recovered starting material (93 mg), 3-(p-bromophenyl)-5-phenylisoxazole (IVb, 53 mg) was isolated (83% yield based on reacted starting material). This sample had m.p. 179—180° (lit. 6 m.p. 178—179°) and was identical (m.p., mixture m.p., infrared spectrum, TLC) with the sample prepared by base-catalyzed elimination from IIIb (see above).

By the above procedure, the following isoxazoles were prepared (yields are based upon reacted starting material):

IVa: 48%, m.p. 141—142° (lit. 4 m.p. 140—141°).

IVc: 55%, m.p. 177—178° (lit. 4 m.p. 178—179°).

IVe: 48%, m.p. 128—129° (lit. 5 m.p. 130°).

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4. Posen, T. Ber. 34 (1901) 3973.

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* For a discussion of the multiplicity (i.e. singlet vs. triplet) of the excited state responsible for the hydrogen abstraction process see Ref. 2c, pp. 384—385.