2-(4-Toluenesulphonyl)-3-aryloxaziridines as Oxidizing Reagents for P(III) Compounds

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2-(4-Toluenesulphonyl)-3-aryloxaziridines, Oxidizing Reagent, Phosphites, Relative Oxidation Rates

The preparation of four 2-(4-toluenesulphonyl)-3-aryloxaziridines by oxidation of the corresponding imines by peracids is described. The relative oxidation rates of trimethyl phosphite by these oxaziridines are determined.

Until recently, no generally applicable oxidizing reagents were known for P(III) compounds, although P(III) compounds are readily oxidized to form the corresponding P(V) compounds. All of the oxidizing reagents that were tested, e.g. hydrogen peroxide [1], aqueous iodine [2], nitrogen oxides [3], 3,3-dimethyloxirane, stilbenene ozonide [4], m-chlorperbenzoic acid [5], tetrabutylammonium periodate, diacetoxyiodosobenzene [6], dimethyl selenoxide [7] and bis(trimethylsilyl)peroxide [8] have a limited scope as oxidizing reagents for P(III) compounds.

In 1972, a kinetic study of the deoxygenation of 2-alkyl-3-aryloxaziridines by tributylphosphine was described [9]. For a long time, the oxidation of P(III) compounds by oxaziridines seems to have been neglected, although there has been considerable interest in the oxidation of olefins and thioethers by oxaziridines [10].

In 1988, it was noticed that P(III) compounds 1 are smoothly oxidized by oxaziridines 2 with electron-withdrawing groups R2, R3 [11].

\[
\begin{align*}
\text{H}_2\text{C} \cdots \text{SO}_2 \cdots \text{N} = \text{S} = \text{O} &+ \text{O} = \text{C} \cdots \text{N} \\
\text{H}_2\text{C} \cdots \text{SO}_2 \cdots \text{N} = \text{H} &+ \text{C} \cdots \text{S} \\
\text{H}_2\text{C} \cdots \text{SO}_2 \cdots \text{N} &+ \text{O} = \text{C} \cdots \text{N}
\end{align*}
\]

Scheme 2. Synthesis of the sulphonylimines 8 and toluenesulphonyl-oxaziridines 9.

The intermediacy of a phosphorane derivative 3 (R’ = OEt; R2 = Ph; R3 = Pr) was observed by \(^{31}\text{P}\) NMR \((\delta = 19.52 \text{ ppm}, \text{H}_3\text{PO}_4)\) when triethyl phosphite was oxidized by 2 (R2, R3 as above) in CDCl3 [11].

Recently, the racemates of diastereomer mixtures of P(III) compounds were reacted with chiral oxaziridines, and stereoselective destruction [12] of one stereoisomer was observed [13].

In the present communication we would like to report on the syntheses of 2-(4-toluenesulphonyl)-3-aryloxaziridines (9).

These oxaziridines can be used as widely applicable oxidizing reagents of P(III) compounds.
The oxaziridines 9 are conveniently prepared by reacting 6 with 7 by heating under reflux in toluene to form 8 [14]. The sulphonylimine 8 is oxidized by 3-chloroperbenzoic acid (MCPBA) or magnesium monoperoxyphthalate (MgMPP) in a two-phase system (aqueous sodium hydrogen carbonate/dichloromethane) at 20 °C.

The versatility and usefulness of 9a-e as oxidizing reagents for P(III) compounds depends on the solubility of the oxaziridines and of the corresponding imines 8. Since 9d and 9e, as well as their imines 8d and 8e, are well soluble in organic solvents like dichloromethane, chloroform, methanol, aceton etc., the oxaziridines 9d and 9e are particularly suitable as oxidizing reagents. Based on reactivity (see Table I) and solubility, 9d is the most promising oxidizing reagent among 9a-e. Therefore 9d and its properties are described in detail in this paper.

Table I. Relative rate constants of the oxidation of trimethyl phosphite by 9a-e.

<table>
<thead>
<tr>
<th>A/B</th>
<th>k_A/k_B</th>
</tr>
</thead>
<tbody>
<tr>
<td>9a/9e</td>
<td>1.66</td>
</tr>
<tr>
<td>9b/9a</td>
<td>1.49</td>
</tr>
<tr>
<td>9b/9c</td>
<td>1.03</td>
</tr>
<tr>
<td>9b/9d</td>
<td>1.06</td>
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<tr>
<td>9b/9e</td>
<td>3.17</td>
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<td>9c/9a</td>
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<tr>
<td>9c/9e</td>
<td>3.22</td>
</tr>
<tr>
<td>9d/9a</td>
<td>1.56</td>
</tr>
<tr>
<td>9d/9e</td>
<td>3.29</td>
</tr>
</tbody>
</table>

In order to check the scope and limitations of the oxaziridines as oxidants for P(III) compounds, 9a-e were reacted with trimethyl phosphite, tri-n-propyl phosphite, triphenyl phosphine and various nucleoside phosphites. Under the conditions of our experiments the oxidation of all P(III) compounds by 9a-e proceeds very rapidly and is generally completed in less than a minute.

The relative rate constants of the oxidation of trimethyl phosphite by 9a-e (see Table I) were determined in competition experiments. For each competition experiment, two oxaziridines 9 were selected. Two equivalents of each of the two oxaziridines 9 were reacted with one mole of trimethyl phosphite in CDCl_3 at 20 °C. The relative amounts of the two imines 8 were determined by comparison of the intensities of the ^1H NMR signals of the imino CH groups of the imines 8 (see Table II).

Completeness of the reaction was checked by ^31P NMR. The relative reaction rates k_A/k_B were computed according to the following eq. [15]:

\[
\frac{k_A}{k_B} = \frac{\ln \left[1 - \frac{a'_{ox}}{a_0}\right]}{\ln \left[1 - \frac{b'_{ox}}{b_0}\right]}
\]

Eq. 1. Determination of the relative reaction rates k_A/k_B.

Here k_A and k_B are the oxidation rates that belong to the oxidants A und B. a_0 and b_0 are the initial ^1H NMR intensities of the oxaziridines A and B, and a'_{ox} and b'_{ox} are the final ^1H NMR intensities of the corresponding imines A' and B'.

The following order of reactivities (see also Table I) corresponds to the influence of the aryl substituents in 9:

4-NO_2 > 4-NC > 2,4-dichloro > 2-NO_2 > 2,6-dichloro 2-nitro- and 2,6-dichlorophenyl oxaziridine are less reactive than 4-nitro-, 4-cyano- and 2,4-dichlorophenyl oxaziridine, although the inductive effect of the substituente is more pronounced in 9a and 9e. The relatively low degree of reactivity of 9a and 9e is probably due to steric hindrance.

It is noteworthy, that 9a-e are the pure E-isomers, whereas the 2-alkyl-3-aryl oxaziridines are generally obtained as mixtures of the E- and Z-isomers [16].

In our next paper on this subject we shall discuss the oxidation of P(III) compounds by 9a-e in greater detail; their use as oxidizing reagents in the synthesis of oligonucleotides by the phosphite amidite method [17] will receive particular attention.

Experimental

NMR spectra were measured with a Bruker AM 360 spectrometer at 360.13 MHz (^1H), 90.556
Comp.  

<table>
<thead>
<tr>
<th>Comp.</th>
<th>CH₃</th>
<th>Tosyl o-H</th>
<th>m-H</th>
<th>H-3</th>
<th>Cl₂Ph H-5</th>
<th>H-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>8d</td>
<td>2.44</td>
<td>7.89</td>
<td>7.36</td>
<td>7.46</td>
<td>7.31</td>
<td>8.08</td>
</tr>
<tr>
<td>s</td>
<td>2H, d</td>
<td>2H, d</td>
<td>d</td>
<td></td>
<td>dd</td>
<td>d</td>
</tr>
<tr>
<td></td>
<td>8.3 Hz</td>
<td>8.3 Hz</td>
<td>2.0 Hz</td>
<td>2.0 Hz</td>
<td>8.5 Hz</td>
<td></td>
</tr>
<tr>
<td>9d</td>
<td>2.48</td>
<td>7.92</td>
<td>7.42</td>
<td>7.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>s</td>
<td>2H, d</td>
<td>3H, m</td>
<td></td>
<td>2H, m</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.4 Hz</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table III. ¹H NMR data (ppm) of 8d and 9d.

MHz (¹³C) and 48.82 MHz (¹⁷O; external standard: H₂O) in CDCl₃. Mass spectra were measured with a Varian CH 5 instrument.

**Preparation of the compounds**

*N-Sulphinyl-4-toluenesulphonamide (TOS–NSO)* (6)

As a modification of the procedure of ref. [14] 6 is purified by recrystallization from hexane/dichloromethane.

*N-(2,4-Dichlorobenzylidene)-4-toluenesulphonamide (8d)*

A solution of 6.0 g (27.6 mmol) of TOS–NSO and 4.8 g (27.6 mmol) of 2,4-dichlorobenzaldehyde in 100 ml dry toluene is heated under reflux for 18 h under a blanket of nitrogen. After evaporation of the solvent, the residue is dissolved in dichloromethane. The product is precipitated by addition of n-hexane and then recrystallized from diethyl ether. 8a–c and 8e were prepared analogously.

Yields, m.p.: **8a**: 70%, 130–132 °C; **8b**: 85%, 203–205 °C [14]; **8c**: 75%, 143–145 °C; **8d**: 81%, 110–111 °C; **8e**: 77%, 113–115 °C.

2-(4-Toluenesulphonyl)-3-(2,4-dichlorophenyl)-oxaziridine (9d)

At 20 °C the solution of 3.8 g (11.0 mmol) MCPPA in 50 ml dichloromethane is slowly added to a stirred two-phase system of 75 ml saturated aqueous NaHCO₃ and a solution of 3.3 g (10.0 mmol) of imine 8d in 50 ml dichloromethane. After about 20 h the organic layer is collected and washed three times with 50 ml saturated sodium chloride solution and then dried over MgSO₄. After evaporation of the solvent the residue is recrystallized from ethyl acetate (variant 1).

When MgMPP is employed as the oxidant, a solution of 10.8 g (17.5 mmol) of MgMPP in 80 ml water is used and 100 ml dichloromethane are added when the reaction is terminated to improve the separation of the layers (variant 2).

9a–c and 8e were prepared analogously.

Yields (variant 1/variant 2), m.p.: **9a**: 88/81%, 150–151 °C; **9b**: 89/82%, 141–142 °C [16]; **9c**: 86/78%, 137–138 °C; **9d**: 91/84%, 126–127 °C; **9e**: 72/50%, 109–110 °C.

9d: MS: no molecular ion; 292/294 (17/6%), 155 (63%), 91 (100%).

C₁₄H₁₁NO₃SCl₂ (344.22)

<table>
<thead>
<tr>
<th>Calcd</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 48.85</td>
<td>48.95</td>
</tr>
<tr>
<td>H 3.22</td>
<td>3.24</td>
</tr>
<tr>
<td>N 4.07%</td>
<td>4.02%</td>
</tr>
</tbody>
</table>

¹³C NMR: 21.85 (Me), 73.23 (C-3), 127.37 (ipso-C, Cl₂Ph), 127.78 (C-5, Cl₂Ph), 129.50, 129.56 (C-3, C-6, Cl₂Ph), 129.59, 130.13 (o-C, m-C, Tos), 130.88 (p-C, Tos), 135.62, 137.59 (C-2, C-4, Cl₂Ph), 146.74 (ipso-C, Tos).

¹⁷O NMR: 140 and 147 (W½ = 390 Hz), SO₂; the oxaziridine-O signal overlaps with the SO₂ signal [18].

All compounds were completely identified. Data are available at request.

**Determination of the relative rate constants for the oxidation of P(III) compounds by the oxaziridines 9a–e**

At 20 °C the solution of 0.02 ml (0.17 mmol) trimethyl phosphite in 1 ml dichloromethane is slowly added to a stirred solution of 0.34 mmol of oxaziridine A and 0.34 mmol of oxaziridine B in 9 ml dichloromethane. After five minutes a sample of 5 ml of the solution is taken, evaporated to dryness and dissolved in 0.5 ml CDCl₃. The ¹H NMR spectra of this solution is measured. The ratios of the imine and oxaziridine protons are obtained for A, B and their imines.

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