The Influence of the Substrate Structure in the Tellurocyclofunctionalization Reaction of \(\gamma,\delta\)-Unsaturated Carboxylic Acids and their Corresponding Benzyl Esters*

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Ácidos carboxílicos \(\gamma,\delta\)-insaturados contendo ligações duplas monosubstituídas reagem com tricloretos de ariltellúrio, fornecendo as telurolactonas esperadas; reação dos ésteres benzílicos correspondentes fornece o produto de adição dos tricloretos de ariltellúrio à ligação dupla. Reação de ácidos carboxílicos \(\gamma,\delta\)-insaturados contendo ligações duplas 1,1-disubstituídas, leva a uma mistura das telurolactonas esperadas e o produto de adição de ácido clorídrico à ligação dupla; os ésteres benzílicos correspondentes fornecem telurolactonas como único produto. A estereoseletividade da reação é baixa; formam-se misturas das duas possíveis lactonas diastereoméricas em relação aproximadamente 1:1.

\(\gamma,\delta\)-Unsaturated carboxylic acids containing monosubstituted double bonds react with aryltellurium trichlorides to give the expected tellurolactone. Reaction of the corresponding benzyl esters gives the addition product of the aryltellurium trichlorides to the double bond. \(\gamma,\delta\)-Unsaturated carboxylic acids containing 1,1-disubstituted double bonds lead to a mixture of the expected tellurolactone and the product of hydrochloric acid addition to the double bond; the corresponding benzyl ester gives the tellurolactone as the only product. The stereoselectivity of the reaction is low; mixtures of the two possible diastereomeric lactones are formed in approximately 1:1 ratios.

Keywords: tellurocyclofunctionalization, tellurolactones

Introduction

The tellurocyclofunctionalization was discovered at the same time as the selenocyclofunctionalization\(^1\). Since then the selenocyclofunctionalization became a valuable synthetic tool\(^2\); however its tellurium counterpart has received relatively little attention. Some time ago we reported a systematic study on the lactonization of \(\gamma,\delta\)-monosubstituted acyclic and cyclic carboxylic acids with \(p\)-methoxyphenylltellurium trichloride\(^3\). The detellurination of the tellurolactones was achieved by \(\text{Bu}_3\text{SnH}\) reduction\(^4\). These are the only reports on the lactonization of unsaturated acids with aryltellurium trichlorides. As several other aspects of this reaction were not yet investigated our group initiated a study to determine the scope and limitations of the tellurolactonization reaction.

In this work we studied the influence of the tellurium electrophile and the olefin structure in the course of the tellurolactonization of \(\gamma,\delta\)-unsaturated carboxylic acids extending the investigation to their benzyl esters. As the reaction leads to mixtures of diastereomeric lactones, the question of the stereoselectivity of this process was addressed.

The \(\gamma,\delta\)-unsaturated carboxylic acids \(1\) and the corresponding benzyl ester \(2\) used are show in Scheme 1.

Two tellurium electrophiles \(p\)-methoxyphenylltellurium trichloride \(3\) and \(p\)-phenoxyphenylltellurium trichloride \(4\)\(^{1d}\) were employed (see Fig. 1).

In all cases, the aryltellurium trichloride \(4\) reacted faster with \(1\) and \(2\) than the aryltellurium trichloride \(3\) (Table 1). Probably this difference in reactivity is associated to the higher solubility of \(4\) in chloroform and the lower electron density on the tellurium atom due to the conjugation of the oxygen lone electron pair with the second phenyl group.

\*Dedicated to Prof. Helena M.C. Ferraz on the occasion of her 50th birthday
The structure of the substrate has a decisive influence in the course of the reaction and in the nature of the products formed. Carboxylic acid 1 reacted with aryltellurium trichloride 3 and 4 leading to the tellurolactone 5a,b in good yields. The corresponding benzyl ester 2 did not give lactones 5a,b. The products were the carbon-carbon double bond adducts with the aryltellurium trichlorides (6) (Scheme 2).

This result can be rationalized in terms of a lower nucleophilicity of the carboxylic oxygen of 2a. Probably the first

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Electrophile</th>
<th>Product</th>
<th>Reaction time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>p-CH3O-O-TeCl</td>
<td>5a</td>
<td>1.7</td>
<td>73</td>
</tr>
<tr>
<td>1a</td>
<td>p-PhO-O-TeCl</td>
<td>5b</td>
<td>0.8</td>
<td>80</td>
</tr>
<tr>
<td>2a</td>
<td>p-CH3O-TeCl</td>
<td>6a</td>
<td>2.5</td>
<td>68</td>
</tr>
<tr>
<td>2a</td>
<td>p-PhO-TeCl</td>
<td>6b</td>
<td>1.5</td>
<td>72</td>
</tr>
<tr>
<td>1b</td>
<td>p-CH3O-TeCl</td>
<td>5c</td>
<td>1.5</td>
<td>74</td>
</tr>
<tr>
<td>1b</td>
<td>p-PhO-TeCl</td>
<td>5d</td>
<td>0.7</td>
<td>83</td>
</tr>
<tr>
<td>1c</td>
<td>p-CH3O-TeCl</td>
<td>5e</td>
<td>2.2</td>
<td>47</td>
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</tbody>
</table>
The hydrochloric acid liberated during the lactone formation attacks the carbon-carbon double bond leading to a tertiary carbenium ion which reacts with the chloride ion giving 7. In the preceding case (Scheme 2) this side reaction was not observed in view of the lower stability of the carbenium ion, which is not formed. This problem could not be circumvented by adding an amine to the reaction me-

Table 1. (cont.)

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Electrophile</th>
<th>Producta</th>
<th>Reaction time (h)</th>
<th>Yieldb (%)</th>
</tr>
</thead>
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<tr>
<td>1c</td>
<td>4</td>
<td>5f</td>
<td>1.2</td>
<td>53</td>
</tr>
<tr>
<td>2c</td>
<td>3</td>
<td>5g</td>
<td>4.2</td>
<td>62</td>
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<tr>
<td>2e</td>
<td>4</td>
<td>5f</td>
<td>3.5</td>
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<td>1d</td>
<td>3</td>
<td>5g</td>
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<tr>
<td>1d</td>
<td>4</td>
<td>5h</td>
<td>1.5</td>
<td>43</td>
</tr>
<tr>
<td>2d</td>
<td>3</td>
<td>5g</td>
<td>4.3</td>
<td>76</td>
</tr>
</tbody>
</table>

aMixture of the two possible diastereomers; bYield of the recrystallized products; cObtained as oils. No satisfactory elemental analysis were obtained.

Scheme 2.

step consists on the formation of a π complex between the double bond and the electrophile. In the absence of a good internal nucleophile, the chloride ion originated from the aryltellurium trichloride attacks the complex leading to the adduct 6.

Reaction of 2 and 4 with acid 1c gave the expected lactone 5e,f accompanied by the carbon-carbon double bond adduct with hydrochloric acid (7) (Eq. 1).
di um to trap the HCl formed since aryltellurium trichlorides react with amines. On the contrary, reaction of 3 and 4 with the benzyl ester 2c gave only the tellurolactones 5e,f in good yields, since benzyl chloride instead of hydrogen chloride was formed as by-product. Similar results were obtained with acid 1d and ester 2d (Table 1).

Concerning the stereochemical course of the reaction it was observed a low stereoselectivity. Acids 1a and 1b gave the tellurolactone in a 3:1 cis/trans ratio. Acids 1c and 1d and esters 2c and 2d gave the tellurolactones in an approximately 1:1 cis/trans ratio (Scheme 3). The electrophile had no influence in the isomeric ratio.

The ratios were determined by NOE experiments with the mixture of isomers and by the relative integral of the methyl groups signals in the 1H-NMR spectra of the crude mixture. In one case (lactone 5e) one isomer was separated by successive recrystallizations and its structure was determined by X-ray analysis. Comparison of the NMR spectrum of the pure isomer 5e with the mixture confirmed the stereochemistry assigned by 1H-NMR analysis.

In conclusion, the tellurolactonization of γ,δ-unsaturated acids containing monosubstituted olefins is successful, the tellurolactonization of γ,δ-unsaturated acids containing disubstituted olefins is not satisfactory leading to a mixture of cyclization products and HCl addition products to the carbon-carbon double bond. However, tellurolactonization of benzyl esters derived from these last acids give good yields of the tellurolactones whereas the benzyl esters derived from the former acids give mixture of products, predominating the carbon-carbon double bond adduct with the aryltellurium trichlorides.

**Experimental**

**General**

Solvents were purified according to the literature. Column chromatography (flash) was performed with 230-400 mesh, 60 Å (Merck) silica gel. TLC was performed on HF-254 (Merck) plates, visualizing with a 254 nm UV lamp and with I2 vapor or with an acidic solution of vanillin. Proton Nuclear Magnetic Resonance spectra (1H-NMR) were recorded on a Bruker AC 200 instrument. The chemical shifts are reported on the δ scale (ppm) downfield from tetramethylsilane. Carbon Nuclear Magnetic Resonance spectra (13C-NMR) were obtained at 50 MHz on a Bruker AC 200 spectrometer and are reported (ppm) relative to the centre line of a triplet at 77.00 ppm for CDC3. Infrared (IR) spectra were measured with a Perkin Elmer

![Scheme 3](image-url)
1750-FT spectrometer. Elemental analysis were performed on a Perkin Elmer 2400 equipment. All analysis were performed by Central Analítica - Instituto de Química - USP.

Tellurium tetrachloride\textsuperscript{1d}, p-methoxyphenylltellurium trichloride\textsuperscript{1d}, p-phenoxypentyltellurium trichloride\textsuperscript{1d}, were obtained by literature procedures.

Reaction of $\gamma,\delta$-unsaturated carboxylic acids (1) with aryltellurium trichlorides (2 or 4)

A mixture of the aryltellurium trichloride (2 or 4) (1.1 mmol) and the $\gamma,\delta$-unsaturated carboxylic acid (1) (1.0 mmol) in dry chloroform (15 mL) was refluxed until the consumption of the starting carboxylic acid. The reaction was monitored by TLC. Then the solvent was evaporated and the residue was filtered through a silica gel column eluting with chloroform. The solution was dried over magnesium sulfate, the solvent was evaporated and the product was recrystallized from chloroform / petroleum ether to give the crude oil with the yields given in Table 1. When the hydrochloric acid aduct was formed it was separated by column chromatography eluting with a mixture of hexane / ethyl acetate (4:1) and then with chloroform to remove the telluroactone.

Reaction of $\gamma,\delta$-unsaturated benzyl esters (2) with aryltellurium trichlorides (2 or 4)

The same procedure described above for the reaction was used. The residue obtained after evaporation of the chloroform was chromatographed on silica gel eluting first with hexane / ethyl acetate (8:1) to remove the benzyl chloride and the non reacted benzyl ester and then with chloroform to remove the tellurated products (5 or 6).

5-[[Dichloro(4-phenoxyphenyl)-\textsuperscript{1H}]]-$\gamma,\delta$-tellanyl[methyl]-3-methyl dihydro-2(3H)-furanone (5a)

\textsuperscript{1H-NMR}, 200 MHz (CDCl\textsubscript{3}) $\delta$ 8.13-8.05 (m, 2 H), 7.10-7.04 (m, 2 H), 5.42-5.31 (m, 1 H), 5.30-5.15 (m, 1 H), 3.92-3.75 (m, 5 H), 2.93-2.80 (m, 1 H), 2.78-2.63 (m, 1 H), 2.33-2.16 (m, 1 H), 1.77 (ddd, $J = 11.5, 10.95, 10.39$ Hz, 1 H), 1.34 (d, $J = 6.54$ Hz, 3 H); \textsuperscript{13}C-NMR, 50 MHz (CDCl\textsubscript{3}) $\delta$ 177.82, 177.38, 162.12, 120.44, 115.56, 115.52, 73.05, 72.60, 55.45, 54.34, 37.68, 36.44, 35.64, 33.41, 15.27, 14.88; IR (cm\textsuperscript{-1}) 3350, 3478, 3415, 1783, 1594, 1571, 1493, 1300, 1261, 1183, 1139, 1029, 1007; Anal. calc. for C\textsubscript{13}H\textsubscript{16}Cl\textsubscript{2}O\textsubscript{3}Te: C, 44.86, H, 3.68; found: C, 44.83, H, 3.51.

5-[[Dichloro(4-methoxyphenyl)-\textsuperscript{1H}]]-$\gamma,\delta$-tellanyl[methyl]-3-methyl dihydro-2(3H)-furanone (5b)

\textsuperscript{1H-NMR}, 200 MHz (CDCl\textsubscript{3}) $\delta$ 8.08 (d, $J = 9.56$ Hz, 2 H), 7.43-7.04 (m, 12 H), 5.58-5.49 (m, 1 H), 5.49-5.29 (m, 1 H), 4.10-3.81 (m, 3 H), 2.93 (ddd, $J = 12.57, 8.52, 5.61$ Hz, 1 H), 2.71 (ddd, $J = 13.28, 8.31, 7.33$ Hz, 1 H), 2.27 (ddd, $J = 12.40, 12.39, 9.99$ Hz, 1 H); \textsuperscript{13}C-NMR, 50 MHz (CDCl\textsubscript{3}) $\delta$ 175.17, 174.80, 160.98, 154.94, 135.82, 135.49, 135.20, 135.15, 134.84, 130.11, 129.08, 128.83, 127.88, 127.69, 124.90, 122.64, 121.94, 120.24, 118.85, 118.79, 73.17, 73.11, 55.72, 54.45, 47.63, 45.04, 38.46, 36.61; IR (cm\textsuperscript{-1}) 3061, 1755, 1755, 1486, 1243, 1197, 1175, 1143, 1006, 697; Anal. calc. for C\textsubscript{18}H\textsubscript{18}Cl\textsubscript{2}O\textsubscript{3}Te: C, 50.86, H, 3.68; found: C, 50.65, H, 3.57.

5-[[Dichloro(4-phenoxyphenyl)-\textsuperscript{1H}]]-$\gamma,\delta$-tellanyl[methyl]-3,5-dimethyl dihydro-2(3H)-furanone (5c)

\textsuperscript{1H-NMR}, 200 MHz (CDCl\textsubscript{3}) $\delta$ 8.11-8.03 (d, 2H), 7.07-7.02 (m, 2 H), 4.09 (d, $J = 11.05$ Hz, 1 H), 3.92 (d, $J = 11.21$ Hz, 1 H), 3.86 (s, 3 H), 3.07-2.85 (m, 1 H), 2.64 (ddd, $J = 13.14, 8.71$ Hz, 1 H), 2.52 (ddd, $J = 12.80, 8.86$ Hz, 1 H), 2.34 (ddd, $J = 12.09, 11.62$ Hz, 1 H), 1.90 (dd, $J = 12.52, 12.15$ Hz, 1 H), 1.87 (s, 3 H), 1.73 (s, 3 H), 1.35 (d, $J = 7.03$ Hz, 3 H), 1.31 (d, $J = 6.96$ Hz, 3 H); \textsuperscript{13}C-NMR, 50 MHz (CDCl\textsubscript{3}) $\delta$ 177.22, 177.12, 162.24, 135.03, 134.97, 134.72, 120.16, 120.01, 115.63, 80.90, 62.52, 61.17, 55.55, 43.92, 43.67, 35.36, 34.88, 29.19, 28.31, 15.22, 14.86; IR (cm\textsuperscript{-1}) 2972, 2939, 1781, 1765, 1585, 1572, 1493, 1455, 1300,
1261, 1183, 1159, 1022; Anal. calc. for C_{14}H_{13}ClO_{2}Te: C, 38.83, H, 4.16; found: C, 38.71, H, 4.12.

5-[[Dichloro(4-methoxyphenyl)-]λ^4-tellanyl[methyl]-5-methyl dihydro-2(3H)-furane (5f)

1H-NMR, 200 MHz (CDCl$_3$) δ 8.14-8.04 (m, 2 H), 7.45-7.05 (m, 7 H), 4.11 (d, J = 11.20 Hz, 1 H), 4.10 (s, 2 H), 3.95 (d, J = 11.22 Hz, 1 H), 3.11-2.85 (m, 1 H), 2.64 (dd, J = 13.16, 8.77 Hz, 1 H), 2.52 (dd, J = 12.81, 8.87 Hz, 1 H), 2.35 (dd, J = 12.14, 11.47 Hz, 1 H), 1.91 (dd, J = 12.48, 11.15, 1 H), 1.87 (s, 3 H), 1.74 (s, 3 H), 1.36 (d, J = 7.06 Hz, 3 H) 1.30 (d, J = 6.97 Hz, 3 H); 13C-NMR, 50 MHz (CDCl$_3$) δ 177.15, 177.04, 161.02, 155.10, 135.28, 135.20, 130.15, 124.94, 122.41, 122.28, 120.27, 118.89, 80.86, 80.83, 62.90, 61.58, 44.01, 43.79, 35.41, 34.93, 29.27, 28.40, 15.27, 14.92; IR (cm$^{-1}$) 2976, 1767, 1596, 1572, 1479, 1236, 1223, 1176, 1170, 1124; Anal. calc.: C, 46.09, H, 4.04; found: C, 45.81, H, 3.96.

5-[[Dichloro(4-phenoxynaphthalene)-]λ^4-tellanyl[methyl]-5-methyl dihydro-2(3H)-furane (5g)

1H-NMR, 200 MHz (CDCl$_3$) δ 8.14-8.07 (m, 2 H), 7.41-7.26 (m, 5 H), 7.10-7.04 (m, 2 H), 4.22 (dd, J = 12.35, 8.88 Hz, 1 H), 4.21 (d, J = 11.19 Hz, 1 H), 4.16 (d, J = 11.26 Hz, 1 H), 4.11 (d, J = 11.22 Hz, 1 H), 4.09 (dd, J = 11.25, 9.27 Hz, 1 H), 4.02 (d, J = 11.07 Hz, 1 H), 3.87 (s, 3 H), 2.92 (dd, J = 13.25, 8.88 Hz, 1 H), 2.82 (dd, J = 11.5, 10.9 Hz, 1 H), 2.76 (dd, J = 13.20, 9.50 Hz, 1 H), 2.39 (dd, J = 12.86, 12.77 Hz, 1 H), 1.93 (s, 3 H), 1.83 (s, 3 H); 13C-NMR, 50 MHz (CDCl$_3$) δ 174.61, 162.30, 135.73, 135.55, 135.10, 135.03, 128.98, 128.92, 128.34, 128.13, 127.89, 127.82, 120.00, 115.70, 81.05, 65.24, 60.94, 55.58, 49.63, 46.16, 44.70, 44.57, 29.21, 28.25; IR (cm$^{-1}$) 1777, 1585, 1494, 1259, 1185, 1110; Anal. calc. for C$_{13}$H$_{24}$O$_{3}$Te: C, 46.09, H, 4.04; found: C, 45.95, H, 4.03.

5-[[Dichloro(4-methoxyphenyl)-]λ^4-tellanyl[methyl]-5-methyl dihydro-2(3H)-furane (5h)

1H-NMR, 200 MHz (CDCl$_3$) δ 8.15-8.09 (m, 2 H), 7.45-7.05 (m, 12 H), 4.23 (d, J = 11.02 Hz, 1 H), 4.21 (dd, J = 13.13, 9.84 Hz, 1 H), 4.18 (d, J = 9.84 Hz, 1 H), 4.11 (d, J = 10.86 Hz, 1 H), 4.05 (dd, J = 11.37, 7.97 Hz, 1 H), 4.03 (d, J = 11.32 Hz, 1 H), 2.91 (dd, J = 13.55, 8.88 Hz, 1 H), 2.81 (dd, J = 11.5, 10.9 Hz, 1 H), 2.77 (dd, J = 13.20, 9.50 Hz, 1 H), 2.40 (dd, J = 12.86, 12.77 Hz, 1 H); 13C-NMR, 50 MHz (CDCl$_3$) δ 174.50, 161.00, 155.05, 135.70, 135.59, 135.49, 135.29, 135.22, 134.98, 134.92, 130.12, 128.98, 128.92, 128.32, 127.89, 127.83, 124.92, 122.30, 120.03, 120.36, 120.24, 118.87, 118.66, 80.98, 80.92, 62.79, 61.24, 46.90, 46.13, 44.74, 44.57, 29.22, 28.26; IR (cm$^{-1}$) 1779, 1575, 1485, 1284, 1245, 1199, 1174, 1124; Anal. calc. for C$_{24}$H$_{23}$ClO$_{2}$Te: C, 51.74, H, 3.95; found: C, 51.54, H, 3.97.

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References


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