The Reaction of 1-Tetralones with Thallium Trinitrate Supported on Clay: Ring Contraction vs α-Oxidation

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A reação de uma série de 1-tetralonas com trinitrato de tâlio adsorvido em Montmorillonita K-10 forneceu produtos de contração de anel (1-indanocarboxilatos de metila) e/ou α-oxidação (2-métóxi-1-tetralonas), em rendimentos bastante variáveis.

The reaction of a series of 1-tetralones with thallium trinitrate supported on Montmorillonite K-10 clay led to products of ring contraction (methyl indan-1-carboxylates) and/or α-oxidation (2-methoxy-1-tetralones), in variable yields.

Keywords: thallium trinitrate, Montmorillonite K-10, ring contraction, α-oxidation, indans

Introduction

The indan system occurs in several natural products of biological relevance. The most common approaches for synthesizing such molecules are either the direct modification of substrates that already bear the indan skeleton or the cycloadition reactions1.

In a previous paper, we have reported the preparation of the hydrindan system by thallium trinitrate (TTN) mediated ring contraction of 2-decalones2. Similarly, functionalized indans were prepared from 3-alkenols3a or from 1,2-dihydropyrene-6-carboxylic acid3b.

The comparison between the prices of 1-tetralones and 1-indanones4, as well as our long standing interest in the thallium(III) chemistry5, prompted us to investigate the application of the methodology above mentioned for the transformation of 1-tetralones into indan derivatives.

There are only two papers regarding the reaction of tetralones with thallium(III) salts. Taylor et al.6, in a communication during the seventies, reported that 1-tetralone (1) is converted into a complex mixture of more than 10 products, when treated with TTN in methanol. However, products of ring contraction 2 and of α-oxidation 3 were isolated, in 1:1 ratio, using TTN adsorbed on Montmorillonite K-10. Unfortunately, the authors did not provide experimental information, such as time, molar ratio of TTN, temperature and solvent (there is only an indication that it was employed an inert one).

The other work dealing with the reaction of tetralones with thallium(III) salt, published in 19907, reported that the treatment of 6-methoxy-1-tetralone (7 in Scheme 4) with TTN in acetic acid gives 2,2-dinitrato-6-methoxy-1-tetralone, as the only isolated product, in 10% yield.

Results and Discussion

The reaction of 1-tetralone (1) was first performed with TTN.3H2O in CH2Cl2, which was in our hands the best condition for the ring contraction of cyclohexanones8 and 2-decalones2. Unfortunately, the reaction furnished a complex mixture of products.

Reinvestigating the previously reported6 reaction of 1-tetralone (1) with TTN/K-10, we observed that the ratio between the products of ring contraction 2 and of α-oxidation 3 increased to at least 5:1, using excess (2 eq.) of the oxidant and pentane as solvent (Scheme 1). We were unable to increase the total yield of this reaction even after several attempts, due to the formation of decomposition products.

\[ \text{Scheme 1.} \]

\[ \text{a) 2 eq. TTN.3MeOH/K-10, pentane, 30 h, rt} \]
The same reaction conditions were then applied to more complex substrates. Of particular interest are those bearing groups at the aliphatic ring, such as 4-methyl-1-tetralone (4), in order to check the stereoselectivity of the rearrangement. Contrary to the reaction of 4-methylcyclohexanone with TTN, whose major product was the cis carboxylic acid\(^a\) (Scheme 2), 4-methyl-1-tetralone (4) furnished a 3:1 mixture of trans:cis diastereomeric esters 5, in 59% yield (Scheme 3). The oxo-oxidation product 6 has also been isolated from the crude reaction mixture in 7% yield.

Interestingly, McKillop’s mechanism\(^9\) explains the observed diastereoselectivity in the ring contraction of 4-methylcyclohexanone, while Wiberg’s mechanism\(^10,11\) justifies the diastereoselectivity for 4-methyl-1-tetralone. We believe that these differences are a consequence of the different migratory aptitudes in each ketone. It is noteworthy that the reaction conditions (TTN.3H\(_2\)O in CH\(_2\)Cl\(_2\) and TTN.3MeOH in pentane) do not change the diastereoselectivity of the thallium(III) promoted rearrangement\(^\text{2}\).

The influence of a methoxy group attached to the aromatic ring in the course of the reaction was also investigated. Although it could be expected a priori that electron-releasing groups at para position would favor the rearrangement, this relationship did not seem to be straightforward for the two substrates tested. Thus, 6-methoxy-1-tetralone (7) furnished only the ring contraction product 8, in moderate yield (49% after purification), while substrate 9 gave rise to the cis and trans 2-nitrate-1-

tetralones 10, together with 60% of recovered starting material (Scheme 4).

![Scheme 2](image1.png)

**Scheme 2.**

![Scheme 3](image2.png)

**Scheme 3.**

A lower migratory aptitude would be expected for tetralones bearing a methoxy group at meta position. In fact, the reaction of 7-methoxy-1-tetralones 11 and 13, under similar experimental conditions, did not afford any rearrangement product. Both the substrates furnished a mixture of compounds, from which it was possible to isolate only 2-methoxy-1-tetralones 12 and 14, respectively. 5-Methoxy-1-tetralone (15) showed lower reactivity, since 33% of the starting material was recovered even after 3 days under reaction (Scheme 5). Similar results were obtained performing this reaction in THF and in CH\(_2\)Cl\(_2\).

![Scheme 4](image3.png)

**Scheme 4.**

![Scheme 5](image5.png)

**Scheme 5.**
It is important to mention that Ciattini et al. 12 have reported the reaction of a series of 4-chromanones with TTN, either in methanol/HClO₄ or in trimethyl-orthoformate. Some substrates were converted into intractable mixtures, while others furnished products of α-oxidation and/or rearrangement in variable yields. The main conclusion that can be reached from this work is that the behavior of the differently substituted chromanones toward TTN is not straightforward.

Similarly, from our results the only possible generalization is that the ring contraction is not always the preferable pathway in the thallium(III)-mediated oxidation of 1-tetralones.

Despite the fact that the ring contraction products were obtained only in moderate yields, such transformation, developed on commercial available substrates, is still an interesting strategy for the construction of indan systems.

Furthermore, excellent entries for the construction of the indan ring seem to be the dihydronaphtalene systems 3b. The 1,2-dihydronaphtalene (18), for example, furnished as the single isolated product the indan derivative 19 in good yield, when treated with TTN in methanol (Scheme 6).

**Experimental.**

*Caution! Thallium and its salts are toxic and must be handled with care.*

1-Tetralones 1, 4, 7, 11 and 15 are commercially available, while 9 and 13 were prepared following the procedure described by Zubaidha *et al.*, starting from 2-methylanisole and succinic anhydride. Thallium(III) nitrate was purchased from Aldrich and was used as received. TTN.3MeOH/K-10 was prepared by the procedure described by Taylor *et al.*, 6 ¹H and ¹³C NMR spectra were recorded on Bruker AC-200, DPX-300 or DRX-500 spectrometer. IR spectra were measured on a Perkin-Elmer 1750-FT. Gas chromatography analyses were performed in a HP-6890 series II.

**General Procedure for the Reaction of 1-Tetralones with TTN.3MeOH/K-10**

A typical procedure is described for the reaction of 1-tetralone (1) with TTN.3MeOH/K-10. To a stirred solution of 1 (0.176 g, 1.20 mmol) in pentane (25 cm³), was added TTN.3MeOH/K-10 (3.6 g, 2.4 mmol). The mixture was stirred for 30 h and the resulting suspension was filtered, washed with water, then with brine and dried over anhydrous MgSO₄. The crude product was purified through column chromatography (silica gel 230-400 Mesh, hexane-ethyl acetate, gradient elution 0-50%), affording 2₁⁴ (0.081 g, 0.46 mmol, 38%) and 3¹³ (0.015 g, 0.085 mmol, 7%).

**Reaction of 4-Methyl-1-tetralone (4) with TTN.3MeOH/K-10**

The reaction of 4 was performed following the general procedure, using 4-methyl-1-tetralone (0.120 g, 0.749 mmol), pentane (20 cm³) and TTN.3MeOH/K-10 (2.2 g, 1.5 mmol), and stirring for 2 hours. The crude product (0.144 g) was further purified by column chromatography (silica gel 230-400 Mesh, hexane-ethyl acetate, gradient elution 0-50%) affording 5ₐ and 5ₖ (0.081 g, 0.46 mmol, 59%) and cis-2-methoxy-4-methyl-1-tetralone (6) (0.010 g, 0.053 mmol, 7%) as a colorless oil: ¹H NMR (200 MHz, CDCl₃) δ 1.46 (d, J 6.6 Hz, 3H), 1.77-1.96 (m, 1H), 2.46 (dt, J 5.1 and 13.2 Hz, 1H), 3.15-3.26 (m, 1H), 3.63 (s, 3H), 4.04 (dd, J 5.1 and 13.2 Hz, 1H), 7.23-7.59 (m, 4H); ¹³C NMR (50 MHz, CDCl₃) δ 20.7, 32.9, 38.1, 58.2, 81.7, 126.5, 126.7, 127.5, 131.7, 133.7, 142.7, 196.5. The stereochemistry of 6 was determined by comparison with the analogous cis and trans hydroxy derivatives 17.

**Methyl 5-methoxy-1-indanecarboxylate (8)**

The preparation of 8 was performed following the general procedure, using 6-methoxy-1-tetralone (0.086 g, 0.49 mmol), pentane (15 cm³) and TTN.3MeOH/K-10 (1.5 g, 1.0 mmol), and stirring for 5 hours. The crude product (0.110 g) was further purified by column chromatography (silica gel 230-400 Mesh, hexane-ethyl acetate, gradient elution 0-50%), affording the ester 8ₐ (0.048 g, 0.23 mmol, 49%).

**Reaction of 4,7-Dimethyl-6-methoxy-1-tetralone (9) with TTN.3MeOH/K-10**

The reaction of 9 was performed following general procedure, using 4,7-dimethyl-6-methoxy-1-tetralone...
(0.112 g, 0.550 mmol), pentane (20 cm$^3$) and TTN.3MeOH/K-10 (1.6 g, 1.1 mmol), and stirring for 48 hours. The crude product (0.130 g) was purified by column chromatography (silica gel 230-400 Mesh, hexane-ethyl acetate, gradient elution 0-50%) affording 10 (0.039 g, 0.15 mmol, 27%) and the starting material (0.067 g, 0.33 mmol, 60%).

2.7-Dimethoxy-1-tetralone (12)

The preparation of 12 was performed following the general procedure, using 7-methoxy-1-tetralone (0.141 g, 0.800 mmol), pentane (20 cm$^3$) and TTN.3MeOH/K-10 (2.4 g, 1.6 mmol), and stirring for 6 hours. The crude product (0.115 g) was further purified by column chromatography (silica gel 230-400 Mesh, hexane-ethyl acetate, gradient elution 0-50%), affording 12 (0.063 g, 0.30 mmol, 38%) as a pale yellow oil: $\nu_{\text{max}}$/cm$^{-1}$ 2938, 2834, 1694, 1497, 1034 (film); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 2.14-2.22 (m, 1H), 2.34-2.39 (m, 1H), 2.92-2.98 (m, 1H), 3.07 (dt, J 5.0 and 13.6 Hz, 1H), 3.57 (s, 3H), 3.84 (s, 3H), 3.90 (dd, J 4.2 and 10.6 Hz, 1H), 7.00 (s, 1H), 7.42 (s, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 26.5, 29.7, 55.5, 58.2, 81.3, 109.5, 122.1, 129.8, 132.7, 136.1, 158.5, 196.5; m/z 206 (M$,^+$ 6%), 176 (100), 148 (21). 120 (88), 115 (10), 103 (11), 91 (27), 77 (26), 51 (23).

Reaction of 7-Methoxy-6-methyl-1-tetralone (13) with TTN.3MeOH/K-10

The reaction of 13 was performed following the general procedure, using 7-methoxy-6-methyl-1-tetralone (0.152 g, 0.797 mmol), pentane (25 cm$^3$) and TTN.3MeOH/K-10 (2.4 g, 1.6 mmol), and stirring for 48 hours. The crude product (0.153 g) was purified by column chromatography (silica gel 230-400 Mesh, hexane-ethyl acetate, gradient elution 0-50%) affording 14 (0.047 g, 0.22 mmol, 27%) and the starting material (0.053 g, 0.28 mmol, 35%). 2,7-Dimethoxy-6-methyl-1-tetralone (14): white solid; mp 67-68 °C; Found: C, 70.49; H, 7.22. Calc. for C$_{13}$H$_{16}$O$_3$: C, 70.89; H, 7.32. $\nu_{\text{max}}$/cm$^{-1}$ 2929, 2843, 1689, 1457, 1264 (CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 2.12-2.20 (m, 1H), 2.24 (3H), 2.32-2.38 (m, 1H), 2.88-2.94 (m, 1H), 3.00-3.05 (m, 1H), 3.57 (3H), 3.86 (s, 3H), 3.90 (dd, J 4.2 and 10.6 Hz, 1H), 7.00 (s, 1H), 7.42 (s, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 16.6, 26.5, 29.8, 55.6, 58.2, 81.6, 107.1, 130.6, 130.7, 134.2, 136.0, 158.6, 196.4; m/z 220 (M$,^+$ 10%), 205 (1), 190 (100), 177 (2).
6. Taylor, E. C.; Chiang, C.-S.; McKillop, A.; White, J.
   **1972**, *37*, 3381.
11. For a discussion concerning the mechanisms, see reference 8.

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