

Allylic Chlorination of Terpenic Olefins using a Combination of MoCl₅ and NaOCl

Brahim Boualy, Larbi El Firdoussi,* Mustapha Ait Ali and Abdellah Karim

Laboratoire de Chimie de Coordination, Département de Chimie, Faculté des Sciences Semlalia,
Université Cadi Ayyad, PB 2390, 40000 Marrakech, Morocco

MoCl₅ é usado como eficiente agente na cloração alílica de olefinas terpênicas na presença de NaOCl como doador de cloro. Vários terpenóides são convertidos aos cloretos de alila correspondentes em moderados a bons rendimentos em condições reacionais brandas e otimizadas. Diferentes precursores de molibdênio são estudados. Dentre eles, MoO₃ fornece bom rendimento, mas depois de um tempo de reação maior.

MoCl₅ is applied as efficient agent in allylic chlorination of terpenic olefins in the presence of NaOCl as chlorine donor. Various terpenes are converted to the corresponding allylic chlorides in moderate to good yield under mild and optimized reaction conditions. Different molybdenum precursors are also studied. Among them, MoO₃ gives good yield, but after a longer reaction time.

Keywords: monoterpenes, allylic chlorination, molybdenum, sodium hypochlorite

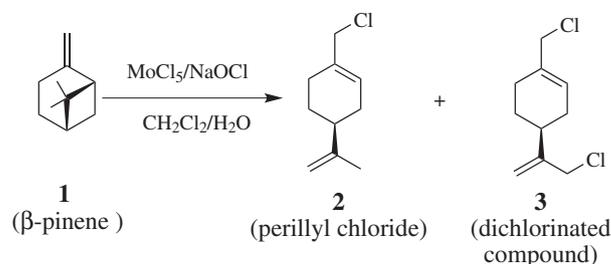
Introduction

Allylic chlorinated terpenes represent a sustainable supply of intermediates for several segments of the fine chemical industry, *e.g.*, the manufacture of flavors and fragrances.¹⁻⁴ Previously, we have reported that allylic amines, alcohols, ketones and alkoxy carbonyl derivatives can be obtained in good yields by the metal complex catalyzed amination, oxidation and alkoxy carbonylation of some monoterpenes.⁵⁻⁷ Chlorination represents a valuable pathway to produce versatile starting materials that are widely used in synthetic organic chemistry.⁸⁻¹¹ Chloride compounds can be prepared directly by bubbling molecular chlorine, but the difficulty of handling chlorine gas limits this procedure.¹² Other authors have shown a convenient method for this transformation using solid CO₂ and calcium hypochlorite^{13,14} or a combination of Vilsmeier reagent and H₂O₂.¹⁵ However, this procedure is limited to non acid-sensitive substrates.¹⁵ CeCl₃ or InCl₃ combined with NaOCl have been reported as efficient systems for allylic chlorination of terminal olefins.¹²⁻¹⁶

In line with our continuous interest in the functionalization of natural terpenic olefins,⁵⁻⁷ we report here the result of our investigation on the allylic chlorination using a combination of sodium hypochlorite and molybdenum pentachloride.

Results and Discussion

In order to optimize the allylic chlorination of natural terpenes, β-pinene **1** was chosen as a model substrate (Scheme 1). The reaction was conducted firstly using various concentrations of MoCl₅ in the presence of NaOCl at room temperature in different reaction times (Table 1).



Scheme 1. Allylic chlorination of β-pinene promoted by molybdenumchloride.

To confirm the role of molybdenum pentachloride, a blank reaction was carried out under similar reaction conditions with β-pinene **1** as substrate. In the presence of NaOCl, no corresponding chlorinated product was observed even after stirring for a long reaction time (entry 1). The same result is observed when using MoCl₅ without NaOCl (entry 2) even at high temperature (80 °C). As has been previously reported, chlorine is usually generated from

*e-mail: elfirdoussi@ucam.ac.ma

Table 1. Allylic chlorination of β -pinene **1** with MoCl₅/NaOCl

| entry | Equiv. of MoCl ₅ | time / min | Conversion ^a / % | Isolated yield / % | |
|----------------|-----------------------------|------------|-----------------------------|--------------------|----|
| | | | | 2 | 3 |
| 1 | 0 | 120 | 0 | 0 | 0 |
| 2 ^b | 0.5 | 120 | 0 | 0 | 0 |
| 3 | 0.5 | 30 | 87 | 67 | 0 |
| 4 | 1.0 | 30 | 89 | 62 | 13 |
| 5 | 1.5 | 30 | 93 | 28 | 58 |
| 6 | 2.0 | 15 | 100 | Complex mixture | |

Conditions: β -pinene (0.5 mmol), NaOCl (2 mmol) in 20 mL of a mixture of CH₂Cl₂/H₂O (1/1) at room temperature. ^aConversion is determined by GC; ^breaction conducted without NaOCl.

sodium hypochlorite.¹²⁻¹⁶ This investigation shows clearly the role of MoCl₅/NaOCl system in the activation and orientation of the reaction toward the desired product.

As it can be seen in Table 1, the stoichiometry of the reaction is also a key point. Using 0.5 equivalent of MoCl₅, perillyl chloride **2** was obtained selectively in 67% yield after 30 min (entry 3). The replacement of MoCl₅ by CeCl₃ under similar reaction conditions gives the same product in only 32% yield. When it was used more than 0.5 equiv. of MoCl₅, both mono- and dichlorinated compounds **2** and **3** were obtained with a variable ratio (entries 4 and 5). At higher amounts of MoCl₅ (2 equiv.), the selectivity decreases considerably (entry 6).

It appears from these results that dichlorinated compound **3** formation is related to the use of high amount of MoCl₅. In this context, Ceschi *et al.*¹⁶ have already shown that the conversion of β -pinene to the dichlorinated product was achieved using InCl₃ or CeCl₃ in a longer reaction time. Liu *et al.*¹⁷ has reported that both α -pinene and β -pinene led to quantitative formation of monochlorinated compounds in DMSO as solvent and phenyldichlorophosphate or phosphorus oxychloride as chlorine donor. It can be noted that the obtained compounds **2** and **3** are chiral with respective optical rotation $[\alpha]_D^{20} = -68$ (1.96) and $[\alpha]_D^{20} = -62$ (2.01) in agreement with those reported in the literature.¹⁶

In order to gain a better insight on this point, a kinetic study was carried out with 1.5 equiv. of MoCl₅ using GC (gas chromatography) to determine the conversion and product distribution (Figure 1). As depicted in Figure 1, the evolution of perillyl chloride **2** and **3** versus time, shows that **2** was formed immediately. This compound reached a maximum after 20 min (62%) and then disappeared in favour of **3** whose amount, insignificant at the early stage of the reaction, rapidly increased after 5 min and then much more slowly after 35 min. This observation proves that perillyl chloride **2** behaves, in the presence of an excess amount of MoCl₅, as an intermediate that reacts to give

the dichlorinated **3**, whereas it remains stable when using 0.5 equiv. of MoCl₅.

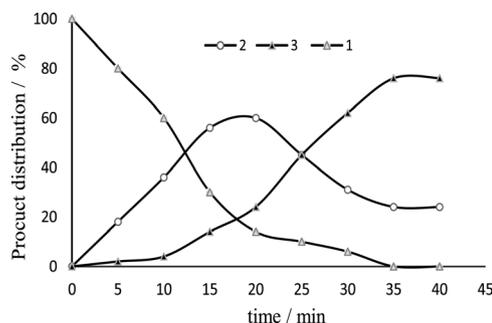


Figure 1. Chlorination of β -pinene with MoCl₅/NaOCl system; product distribution vs. time determined by GC. Conditions: β -pinene (0.5 mmol), MoCl₅ (0.75 mmol), NaOCl (2 mmol) in 20 mL of a mixture of CH₂Cl₂/H₂O (1/1) at room temperature.

A study of the influence of the nature of the molybdenum precursor is reported in Table 2. Among the Mo compounds studied, MoCl₅ appears the most suitable (entry 3). MoO₃ gives good yield but only after a long reaction time (entry 7). In order to confirm the low activity of MoO₃, other terpenes were checked, such as carvone and limonene with MoO₃/NaOCl (0.5 equiv. of MoO₃) under similar conditions. The reaction took place, although in low yields and after 24 h (30 and 19%, respectively). Other sources of Mo present very low activity (entries 9 and 10).

Table 2. Allylic chlorination of β -pinene by different sources of molybdenum

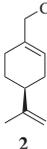
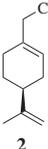
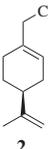
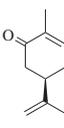
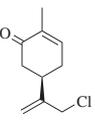
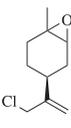
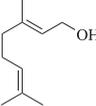
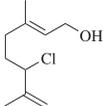
| entry | Lewis acid (equiv.) | time / h | Conversion ^a / % | Isolated yield / % |
|-------|---|----------|-----------------------------|--------------------|
| 3 | MoCl ₅ (0.5) | 0.5 | 87 | 67 |
| 7 | MoO ₃ (0.5) | 4 | 100 | 83 |
| 8 | MoO ₃ (1) | 2.5 | 100 | 78 |
| 9 | C ₁₀ H ₁₄ MoO ₆ (1) | 4 | 21 | 14 |
| 10 | Mo(acac) ₃ (1) | 4 | 19 | 16 |
| 11 | (NH ₄) ₆ Mo ₇ O ₂₄ (1) | 24 | 0 | 0 |

Conditions: β -pinene (0.5 mmol), NaOCl (2 mmol) in 20 mL of a mixture of CH₂Cl₂/H₂O (1/1) at room temperature. ^aConversion is determined by GC.

To assess the scope and limitation of this reaction, different monoterpenes were studied (Table 3). With MoCl₅/NaOCl system under the optimized β -pinene conditions, all the substrates are converted to the corresponding chlorinated products in good to excellent yields.

α -Pinene **4** gave perillyl chloride **2** selectively (entry 12). However, both mono- and dichlorinated products **2** and **3** were obtained with the increasing of the amount of MoCl₅ (1 equiv.) (entry 13). Entry 14 shows good conversion of limonene **5** to

Table 3. Allylic chlorination of natural terpenes by MoCl₅/NaOCl

| entry | Olefins | Products | $[\alpha]_D^{20}$ (concentration) | Isolated yields / % | Ref. |
|-----------------|---|---|-----------------------------------|---------------------|--------|
| 12 ^a |  4 |  2 | -67 (1.95) | 75 | 16 |
| 13 ^b |  4 |  2 | 2: -67 (1.95) 3: -58 (1.73) | 2: 58 3: 13 | 16 |
| 14 |  5 |  2 | 2: -88 (2.13) 3: -83 (1.91) | 2: 38 3: 21 | 16 |
| 15 |  6 |  7 | -56 (2.13) | 87 | 14, 18 |
| 16 |  8 |  9 | -43 (2.0) | 68 | 14, 18 |
| 17 |  10 |  11 | - | 51 | 16 |

Conditions: olefin (0.5 mmol); MoCl₅ (0.25 mmol); NaOCl (2 mmol) in 20 mL of a mixture of CH₂Cl₂/H₂O (1/1); 30 min at room temperature. ^aReaction conducted at 0 °C for 6 h; ^bwith 0.5 mmol of MoCl₅.

the same products **2** and **3** in 38 and 21% yields, respectively. The difference of the optical rotation values of **2** and **3** obtained from the chlorination of pinenes and limonene is due to the fact that the ring opening of the pinenes can result in partial racemization. With carvone **6**, limonene oxide **8** and geraniol **10**, the reaction also works well to give the corresponding monochlorinated derivatives (entries 15-17).

Conclusions

In conclusion, we have described an efficient and facile method for the transformation of naturally occurring monoterpenes to the corresponding allylic chlorides using an inexpensive and readily available Lewis acid (MoCl₅). The reaction processes in short reaction time, under mild

conditions to afford the expected products in moderate to good yields. A rearrangement of α -pinene and β -pinene to perillyl chloride is observed. Some other molybdenum precursors have been checked and interesting results have been obtained with MoO₃/NaOCl and β -pinene as substrate. These results lead us to believe that this allylic chlorination method may represent a valuable alternative to the existing procedures reported in the literature.

Experimental

Instruments

NMR studies were performed on a Bruker Avance 300 spectrometer in CDCl₃, chemical shifts are given in ppm

relative to external TMS (tetramethylsilane) and coupling constant (*J*) in Hz. Mass spectra were recorded on AMD 402 spectrometer (70 eV, EI). All the spectroscopic data of the known products were compared with those reported in the literature. The reaction mixtures were analyzed on a Trace GC Thermo Finnigan chromatograph equipped with an FID detector (flame ionization detector). GC parameters for capillary columns BP (25 m × 0.25 mm, SGE): injector 250 °C; detector 250 °C; oven 70 °C for 5 min then 3 °C min⁻¹ until 250 °C for 30 min; column pressure 20 kPa, column flow 6.3 mL min⁻¹; linear velocity 53.1 cm s⁻¹; total flow 138 mL min⁻¹. Optical rotations were measured in an ATAGO polax-D polarimeter with a 0.1 dm cell at a temperature of 20 °C. Liquid chromatography was performed on silica gel (Merk 60, 220-440 mesh; eluent: hexane). Analytical thin-layer chromatography (TLC) was conducted on Merck aluminium plates with 0.2 mm of silica gel 60F-254. All the reagents and solvents used in the experiments were purchased from commercial sources and used as received without further purification (Aldrich, Acros).

General procedure

In a typical experiment, olefin (0.5 mmol) in 10 mL of CH₂Cl₂ was added to a vigorously stirred solution of MoCl₅ (0.25 mmol) in 10 mL of water. It was added 2 mmol (0.95 mL) of NaOCl (13% m/m) To the resulting mixture and the reaction mixture was stirred for 30 min at room temperature. The reaction was quenched by the slow addition of saturated aqueous Na₂SO₃. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL). The combined organic layer was dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure. Pure chlorinated products were obtained by column chromatography over silica gel (weight ratio of silica gel to compound mixture: 220/1) using hexane as eluent. All isolated pure products were fully characterized by ¹H and ¹³C NMR and MS, and then compared with the known compounds.

Supplementary Information

Supplementary information (¹H and ¹³C NMR and MS data for compounds **2**, **3**, **7**, **9** and **11**) is available free of charge at <http://jbcs.org.br> as a PDF file.

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Submitted: October 10, 2010

Published online: March 1, 2011