Conversion of carboxylic acids to amides under the action of tantalum(V) chloride

Azat M. Gabdullin,* Oleg S. Mozgovoj, Rita N. Kadikova, Ilfir R. Ramazanov, Aliya K. Amirova and Usein M. Dzhemilev

Institute of Petrochemistry and Catalysis of Russian Academy of Sciences, 141 Prospekt Oktyabrya, 450075 Ufa, Russia; skill15@mail.ru (O.S.M.); kadikritan@gmail.com (R.N.K); ilfir.ramazanov@gmail.com (I.R.R); alya02265@gmail.com (A.K.A.); ink@anrb.ru (U.M.D.)

* Correspondence: saogabdullinsao@gmail.com

Abstract: It was found that the reaction of aliphatic carboxylic acids with secondary amines under the action of tantalum (V) chloride leads to the selective formation of carboxamides. N,N-Diethyladamantane-1-carboxamide were synthesized with a yield of 73% as well.

Introduction

It is known that tantalum compounds can be useful for the synthesis of various classes of organic compounds. The TaCl₅-Mg reagent system is an effective tool for the reduction of non-functionalized alkynes and 1-alkynyl sulfones to the corresponding olefins [1]. Recently, we have developed a regio- and stereoselective method for the synthesis of substituted 3-alkenyl amines and 4-alkynyloles based on the reduction of alkynyl amines and alcohols using a similar reagent system NbCl₅-Mg [2]. The possibility of creating a new carbon-carbon bond was demonstrated by the example of the TaCl₅-catalyzed carboxamides formation reaction of 1-alkenes with n-alkyl Grignard reagents [3-5]. Thus, low-valence tantalum complexes are effective reagents for the transformation of the triple bond of various acetylenic compounds. The closest electronic analogue of the tantalum atom is niobium. According to [6], NbCl₅ promotes the conversion of carboxylic acids into carboxamides. In this work, in order to study the possibility of conversion of carboxylic acids under the conditions of organotantalum synthesis, we studied the reaction of carboxylic acids with secondary amines in the presence of catalytic amounts of TaCl₅.

Results and discussion

We found that the reaction of carboxylic acids 1 with 3 equivalents of a secondary amine in the presence of 33 mol. % of TaCl₅ in a solution of methylene chloride after refluxing for 5 hours gave amides 2 in 51-87 % yield (Table 1). In the case of amination of heptanoic acid with dibenzylamine, the yield of carboxamide was 51% (Entry 4). Apparently, the decrease in the yield of the formed amide in the case of dibenzylamine is associated with steric hindrances arising from the interaction of heptanoyl chloride formed in situ with dibenzylamine. At present, we have failed to obtain betulinic acid amide in methylene chloride solution. It is possible that the inertness of betulinic acid is caused by the presence of hydroxyl group in the A ring that binds TaCl₅ reagent.

The quantitative formation of oxoniobium and oxotitanium carboxylates as a result of the treatment of carboxylic acids with NbCl₅ and TiCl₄ is described in the literature [7,8]. However, the generation of oxotitaniuam carboxylates requires the use of more amount of carboxylic acid than the formation of oxoniobium carboxylates. At the same time, the effect of steric factors on the yield of the formed amide (31%) was demonstrated by the example of the TiCl₄-promoted amination reaction of pivalic acid using pyrrolidine in a tetrahydrofuran solution [9]. The reaction of pivalic acid with diethylamine in a solution of methylene chloride in the presence of NbCl₅ gave the corresponding amide in 78% yield [6].
Table 1

| Entry | R'OH | R',NH | Isolated yield 2, % |
|-------|------|-------|--------------------|
| 1     | R = nPent | R = nBu | 2a (77) |
| 2     | R = nHept | R = nBu | 2b (81) |
| 3     | R = nHex | R = nBu | 2c (83) |
| 4     | R = nHex | R = Bn | 2d (51) |
| 5     | R = C15H31 | R = nBu | 2e (86) |
| 6     | R = C17H35 | R = nBu | 2f (87) |

TaCl₅-promoted reaction of succinic acid 3 with diethylamine in methylene chloride solution gave dicarboxamide 4 in 53% yield (Scheme 1). In the present work, we also found that the reaction under study allows the selective conversion of 1-adamantanecarboxylic acid under the action of diethylamine to the corresponding amide 5.

Conclusions

Thus, we have demonstrated for the first time that the reaction of aliphatic mono- and dicarboxylic acids with secondary amines under the action of catalytic amounts of tantalum (V) chloride leads to the selective formation of carboxamides.

Experimental section

General information

The carboxylic acids and secondary amines were obtained from Sigma-Aldrich or Acros. Dichloromethane were distilled over P₂O₅. Nuclear magnetic resonance spectroscopy was performed on a Bruker Avance 500. The ¹H NMR spectra were recorded at 500 MHz and ¹³C-{¹H} NMR spectra at 100 MHz in CDCl₃. The chemical shifts are reported in ppm relative to tetramethylsilane (TMS) as the internal standard. The numbering of atoms in the ¹³C-{¹H} and ¹H NMR spectra of the compounds 2a-f, 4, 5 is shown in Figure 1. The reaction mixture was performed using a Carlo-Erba CHN 1106 elemental analyser. Mass spectra were obtained on a Finnigan 4021 instrument. The yields were calculated from the isolated amount of carboxamides obtained from starting 2-alkynylamines.

Preparation of carboxamides 2a-f, 4, 5 via conversion of carboxylic acids to amides under the action of tantalum(V) chloride.
Using the procedure described above 288 mg of octanoic acid (2 mmol) gave crude product that was purified by column chromatography (hexane : ethyl acetate = 5 : 1) to afford 2b (413 mg, 81%) as colorless oil. Rf 0.67.

\[ \text{N,N-dibutylcyclohexylamide (2b)} \]

Using the procedure described above 260 mg of heptanoic acid (2 mmol) gave crude product that was purified by column chromatography (hexane : ethyl acetate = 5 : 1) to afford 2c (400 mg, 83%) as colorless oil. Rf 0.70.

\[ \text{N,N-dibutylheptanamide (2c)} \]

Using the procedure described above 568 mg of stearic acid (2 mmol) and dibutylamine, (258 mg, 5.26 mmol) gave crude product that was purified by column chromatography (hexane : ethyl acetate = 5 : 1) to afford 2f (689 mg, 87%) as colorless oil. Rf 0.69.

\[ \text{N,N-dibutyldodecanamide (2f)} \]

Using the procedure described above 236 mg of succinic acid (2 mmol) and diethylamine, (146 mg, 5.26 mmol) gave crude product that was purified by column chromatography (hexane : ethyl acetate = 5 : 1) to afford 4 (242 mg, 53%) as colorless oil. Rf 0.69.

\[ \text{N,N,N,N'-tetraethylsuccinamide (4)} \]

Using the procedure described above 360 mg of 3(3r,5r,7r)-adamantane-1-carboxylic acid (2 mmol) and diethylamine, (146 mg, 5.26 mmol) gave crude product that was purified by column chromatography (hexane : ethyl acetate = 5 : 1) to afford 5 (343 mg, 73%) as colorless oil. Rf 0.64.

\[ \text{N,N'-diethyladamantane-1-carboxamide (5)} \]
\(^{13}\)C NMR (500 MHz, CDCl\(_3\)): \(\delta = 13.72\) (2C), 28.62 (3C), 36.72 (3C), 38.68, 39.18 (3C), 41.81 (2C), 176.09.

MS (EI): \(m/z, \% = 235\) (22) [M\(^+\)], 206 (5), 135 (100), 93 (12), 79 (14), 41 (6).

Anal. calcd for \(C_7H_9NO\), (%): C, 76.55; H, 10.71; N, 5.95; Found, %: C, 76.61; H, 10.68; N, 4.89.

**Conflicts of interest**
The authors declare no competing financial interest.

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