Synthesis of α-aminophosphonates by Kabachnik-Fields reaction using [Ce(*L*-Pro)]$_2$(Oxa) as a heterogeneous catalyst

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Keywords: α-aminophosphonates, heterogeneous catalyst, one-pot reaction, Kabachnik-Fields.

Abstract

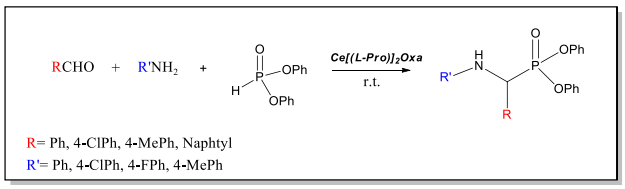
We developed a new catalyst for Kabachnik-Fields reaction, [Ce(*L*-Pro)]$_2$(Oxa), using an accessible, simple and efficient protocol

Introduction

Organophosphorus compounds are useful as building blocks for some compounds that present medicinal applications. This class of compounds had attracted great attention because frequently it has presented some biological properties such as antibacterial, antithrombotic agent, anti-inflammatory, carcinogenic, pesticides and HIV protease.[1] Due to the biological potential of the α-aminophosphonates, it's necessary a methodology that allows the synthesis of them, because many procedures have long reaction times, low yields, utilization of stoichiometric amounts of catalyst and difficulties of separation and the recycling of it.[2] For this reason, herein we presented a simple and efficient methodology for the synthesis of α-aminophosphonates using [Ce(*L*-Pro)]$_2$(Oxa) as a heterogeneous catalyst. This catalyst was separated by filtration and reused other times (Scheme1).

Results and Discussion

The standard reaction was carried out using aniline, benzaldehyde, diphenyl phosphite and 1% mol of catalyst [Ce(*L*-Pro)]$_2$(Oxa) in toluene, based on the methodology described by Zhu[3] and co-workers.



Scheme 1. Synthesis of α-aminophosphonates

We observed that the reaction afforded 96% of yield in short reaction time (10 min). The next step was verify the effect of the solvent over the standard reaction. For this reason, we carried out the standard reaction in THF, CH_3CN, toluene, DCM and the best result obtained was in toluene (96%). After that, we studied the effect of the catalyst loading over the reaction yields. We observed that the increasing of the catalyst (2% mol) did not give a substantial increasing on the yield (98%) and when we carried out this reaction without catalyst, the interest compound was not obtained. Therefore, we extended the procedure for many anilines and benzaldehydes substituted and the data are presented at Table 1.

Table 1. Kabachnik-Fields reaction using [Ce(*L*-Pro)]$_2$(Oxa)

R	R'	Time (min)	Yield (%)
Ph	Ph	10	96
4-NO_2Ph	Ph	10	99
4-ClPh	Ph	10	98
4-OMePh	Ph	60	94
4-MePh	Ph	60	94
Ph	4-NO_2Ph	20	91
Ph	4-ClPh	5	96
Ph	4-OMePh	50	89
Ph	2,6-MePh	60	98

Reaction conditions: benzaldehyde (2.2 mmol), aniline (2.0 mmol) and diphenyl phosphite (2.0 mmol) in toluene and 1 % mol catalyst at r. t.

All compounds were purified by recrystallization and characterized by ^{1}H and ^{13}C NMR spectra and infrared spectra. Besides, we carried the catalyst recycling and we concluded it could be reused for more three cycles.

Conclusion

The [Ce(*L*-Pro)]$_2$(Oxa) was an effective catalyst on the Kabachnik-Fields reactions affording high yields of α-aminophosphontes in short reaction times. Other advantages of this catalyst were its ability to be reused in some cycles, easy preparation and compatibility with wide a range substrate.

Acknowledgements

CNPq, CAPES, UFGD e LACOB.

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