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Lanthanides in Organic Synthesis: Eu^{+3}-Catalyzed Michael Addition of 1,3-Dicarbonyl Compounds

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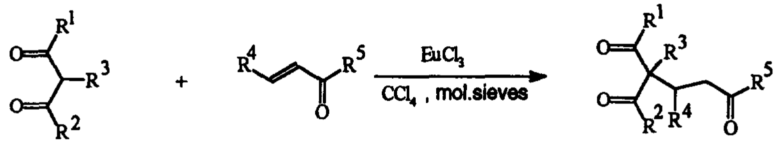
Abstract: $EuCl_3$ proves to be an efficient catalyst for Michael addition of 1,3-dicarbonyl compounds. The employment of Eu^{+3} chiral complex $[Eu(tfc)_3]$ allows the formation of Michael adducts in enantioselective way.

In these last years the lanthanides have received increasing attention both as reagents and catalysts for organic reactions.[1,2] In particular, Eu^{+3} alkoxides and complexes have been used for the achievement of diastereoselective aldol condensation[3], cyanohydrins synthesis[4], enantioselective hetero Diels-Alder[5], etc.

In the course of investigation on the reactivity of active methylene compounds catalyzed by lithium iodide[6], we have found that the easily available hexahydrate europium (III) chloride is an efficient catalyst for the conjugate addition of 1,3-dicarbonyl compounds 1. In fact, in anhydrous CCl_4, in the presence of catalytic amounts of $EuCl_3$ the formation of adducts 3 occurs with very satisfactory yields, as reported for different donors and acceptors in Table 1.



1 2 3

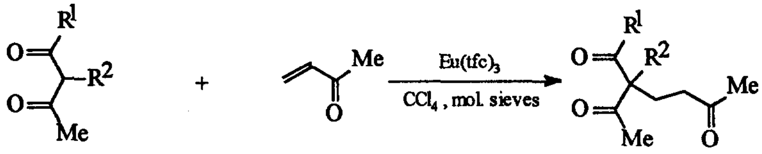
Table 1 - $EuCl_3$-catalyzed Michael addition of 1,3-dicarbonyl compounds

Entry	R^1	R^2	R^3	R^4	R^5	Reac. Time	T (°C)	Yield [a)
1	-OEt	-Me	-H	-H	-Me	24h	r. t.	80%
2	-Ph	-Me	-H	-H	-Me	24h	r. t.	77%
3	-OEt	-Ph	-H	-H	-Me	20h	r. t.	80%
4	-OEt	-Me	-H	$-(CH_2)_3-$		20h	r. t.	71% [b)
5	-OEt	-Me	-Et	-H	-Me	72h	60	65%
6	-OEt	$-(CH_2)_3-$		-H	-Me	48h	60	85%
7	-OEt	-Me	-H	-Ph	-Me	52h	60	61% [b)
8	-OEt	-Me	allyl	-H	-Me	38h	60	54%

[a) All the yields refer to isolated chromatographically pure compounds.

[b) Obtained as 1/1 diastereoisomeric mixture

The very mild conditions allow high selectivity as supported by the absence of the typical side-reactions which can be observed in the conventional base-catalyzed processes (bis-additions, polymerizations, ß-fission, etc.). More interestingly, in the presence of catalytic amount (10%) of tris[3-(trifluoromethylhydroxymethylene)-d-camphorato]europium(III), Eu(tfc)$_3$, conjugate addition of 1,3-dicarbonyl compounds shows to proceed in enantioselective way (Table 2).



1 2 3

Table 2 - Eu(tfc)$_3$-catalyzed enantioselective Michael addition of 1,3-dicarbonyl compounds

Entry	R^1	R^2	T (°C)	Reac. Time	Yield a)	e.e. b)
1	-OEt	-Et	- 33	72h	71%	25%
2	-OEt	-Et	- 25	24h	50%	36% c)
3	-Ph	-Me	- 35	24h	68%	32%
4	-OEt	-Bz	r. t.	24h	36%	23%

a) All the yields refer to isolated chromatographically pure compounds

b) Enantiomeric excesses have been determined by ^{1}H-NMR analysis (solvent C_6D_6) in the presence of Eu(hfc)$_3$ as shift reagent.

c) In this case an increased amount of Eu(tfc)$_3$ has been employed (30%).

It has to be noted that, with the exception of few particular Michael donors,[7,8] the formation of Michael adducts of type 3 takes place with very low degree of enantioselectivity in catalytic reactions.[9]

Experimental: a mixture of 1,3-dicarbonyl compound (5 mmol), Michael acceptor (6 mmol), Eu^{+3} catalyst (0,5 mmol) and activated molecular sieves (1 g), in anhydrous CCl_4 (2.5 ml), is stirred under conditions given in Table 1 and 2. Then,after the usual work-up, the crude adducts 3 are purified by silica gel column chromatography by elution with n-hexane/diethyl ether mixtures.

References and Notes

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