University of Groningen

Zinc(II) Catalysed Conjugate Addition of Grignard Reagents to α,β -Unsaturated Ketones

Jansen, Johan F.G.A.; Feringa, Bernard

Published in:
Journal of the Chemical Society, Chemical Communications

DOI:
[10.1039/c39890000741](https://doi.org/10.1039/c39890000741)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1989

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Jansen, J. F. G. A., & Feringa, B. (1989). Zinc(II) Catalysed Conjugate Addition of Grignard Reagents to α,β -Unsaturated Ketones. *Journal of the Chemical Society, Chemical Communications*, 29(11).
<https://doi.org/10.1039/c39890000741>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Zinc(II) Catalysed Conjugate Addition of Grignard Reagents to α,β -Unsaturated Ketones

Johan F. G. A. Jansen and Ben L. Feringa*

Department of Organic Chemistry, University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands

Zinc(II)-diamine complexes are efficient catalysts for the conjugate additions of Grignard reagents to various α,β -unsaturated ketones.

The conjugate addition of organocuprates,¹ and more recently organozincates² derived from Grignard and organolithium reagents, to α,β -enones comprises useful synthetic methodology. Considerable progress has been achieved in the use of organozincates with non-transferable ligands^{2,3,4} and in enantioselective conjugate additions with organocuprates⁵ and chiral copper catalysts.⁶ Despite the fact that powerful copper(I) catalysed 1,4-additions have been developed^{1,6} the zinc(II) catalysed addition of organometallic reagents has hardly been investigated.[†] We report herein the conjugate addition of Grignard reagents to α,β -enones catalysed by diamine-zinc(II) complexes.

In order to study the effect of zinc complexes in conjugate addition reactions the reaction of ethyl- and isopropyl-magnesium bromide with α,β -unsaturated ketones using 0.1 mol% of tetramethylethylenediaminezinc dichloride [(tmeda)ZnCl₂] (**1**) or (tmeda)Zn(OBu^t)Cl (**2**) was examined (Scheme 1). In a typical experiment PrⁱMgBr (10.5 mmol) in diethyl ether under a N₂ atmosphere was added to a solution of (**1**) or (**2**) (0.01 mmol) in tetrahydrofuran (THF). Cyclohexenone (10 mmol) was slowly added (5 min) and after 30 min the product was isolated using standard procedures.

The results of the conjugate addition with various enones are summarized in Table 1.

Several effects were observed using *catalytic amounts* (0.1 mol%) of zinc complexes at 0 °C. The isolated yields of 1,4-adducts increase substantially in all cases (Table 1). The amount of condensation products, as observed in the uncata-

[†] 1,4-Additions of diethylzincate catalysed by a Ni^{II} complex have recently been reported¹⁰

Scheme 1. Reagents and conditions: RMgBr, THF, 0 °C, catalyst (0.1%), (**1**), (**2**), or (**3**).

Table 1. Conjugate addition of Grignard reagents to enones using (1) and (2) as catalysts.

Entry	Grignard (R in RMgBr)	Enone ^a	Catalyst (1) ^b	Catalyst (2) ^b
			1,4/1,2 (%) ^d ratio ^c	1,4/1,2 (%) ^d ratio ^c
1 ^e	Pr ⁱ	(4)	[3 (25)]	
2 ^{e,f}	Pr ⁱ	(4)	[4.6(25)]	
3	Pr ⁱ	(4)	5.7(81)	19 (88)
4	Et	(4)	1.0(36)	1.4(50) ^g
5	Pr ⁱ	(5)	8.1(34)	9.0(51)
6	Et	(5)	0.9(37)	1.0(48)
7	Pr ⁱ	(6)	7.3(83)	13.4(87)
8	Et	(6)	49 (89)	49 (91) ^g
9	Pr ⁱ	(7)	5.7(42)	6.1(60)

^a Enones: (4), cyclohexenone; (5), but-1-en-3-one; (6), 1-phenylbut-1-en-3-one; (7), cyclopentenone. ^b 0.1 mol% in all cases. ^c Ratios determined by g.l.c. ^d Isolated yields of 1,4-adduct; all compounds showed correct i.r., ¹H and ¹³C n.m.r., and high resolution mass spectral data. ^e No zinc complex catalyst used. ^f PrⁱMgBr, tmeda, KOBu^t. ^g The isolation of 22% and 57% 1,4-adduct from the Grignard addition to (4) and (6) has been reported.⁷

lysed case, is consequently drastically decreased (entry 1). The regioselectivity towards the 1,4-adduct (1,4/1,2 ratio) is considerably increased in all cases using even this small amount of zinc complex; however in some cases (entries 4, 6) improvement is still required for synthetic purposes. Both the isolated yields of 1,4-adducts and the regioselectivity increase further when (tmeda)Zn(OBu^t)Cl (2) is used instead of (tmeda)ZnCl₂ (1) as a catalyst.

We have previously observed a similar effect of an alkoxide as a non-transferable ligand in the stoichiometric conjugate addition of organozincates.³ On the basis of the results presented here it is reasonable to assume that a tmeda-dialkyl zincate in the case of (1) and a tmeda-monoalkylzinc-t-butoxide complex in the case of (2) act as the actual catalytically active species. Surprisingly the isolated yields of 1,4-adducts using catalyst (2) are only slightly lower than the reponed results using stoichiometric trialkylzincates² or mono-alkoxide substituted dialkylzincates.³

The preliminary results of the enantioselective catalytic conjugate addition of PrⁱMgBr to cyclohexenone using the chiral zinc complex (3) are in line with these observations.

Complex (3) is prepared from (*S,S*)-*N,N'*-dimethyl-*N,N'*-bis(1-phenylethyl)-1,2-ethylenediamine.^{3,8} With 1 mol% of (3) at 0 °C we obtained 3-isopropylcyclohexanone with an enantiomeric excess (e.e.) of 8%.[‡] The e.e. was determined by ¹³C n.m.r. of the diastereoisomeric (2*R*,3*R*)-(-)-butane-2,3-diyl acetal.¹¹ This result provides additional support for the catalytic role of the zinc complexes. In conclusion we have observed, as far as we know, the first conjugate addition of Grignard reagents catalysed by zinc complexes.

We thank the Dutch Foundation for Scientific Research (Nederlandse Organisatie voor Wetenschappelijk Onderzoek, N.W.O.) for their financial support of this research.

Received, 31st January 1989; Com. 9/00508K

References

- G. H. Posner, 'An Introduction to Synthesis using Organocopper Reagents,' Wiley, New York, 1980; B. H. Lipshutz, R. S. Wilhelm, and J. A. Kozlowski, *Tetrahedron*, 1984, **40**, 5005.
- M. Isobe, S. Kondo, N. Nagasawa, and T. Goto, *Chem. Lett.*, 1977, 679; W. Tückmantel, K. Oshima, and H. Nozaki, *Chem. Ber.*, 1986, **119**, 1581; R. A. Kijonaas and E. J. Vawter, *J. Org. Chem.*, 1986, **51**, 3993; R. A. Kijonaas and R. K. Hoffer, *ibid.*, 1988, **53**, 4133.
- J. F. G. A. Jansen and B. L. Feringa, *Tetrahedron Lett.*, 1988, **29**, 3593.
- R. A. Watson and R. A. Kijonaas, *Tetrahedron Lett.*, 1986, **27**, 1437.
- K. Koga and K. Tomioka in 'Asymmetric Synthesis,' ed. J. D. Morrison, Academic Press, New York, 1983, Vol. 2, p. 201; S. H. Bertz, G. D. Dabbagh, and G. Sundararajan, *J. Org. Chem.*, 1986, **51**, 4953; F. Leyendecker and D. Lavcher, *Nouv. J. Chim.*, 1985, **9**, 13; E. J. Corey, R. Naef, and F. J. Hannon, *J. Am. Chem. Soc.*, 1986, **108**, 7114; R. K. Dieter and M. Tokles, *ibid.*, 1987, **109**, 2040.
- G. M. Villacorta, Ch. P. Rao, and S. J. Lippard, *J. Am. Chem. Soc.*, 1988, **110**, 3175.
- M. S. Karasch and O. Reinmuth, 'Grignard Reactions of Nonmetallic Substances,' Prentice-Hall, New York, 1954.
- L. Horner and K. Dickerhof, *Liebigs Ann. Chem.*, 1984, 1240.
- W. Langer and D. Seebach, *Helv. Chim. Acta*, 1979, **62**, 1710.
- K. Soai, T. Hayasaka, S. Ugajin, and S. Yokohama, *Chem. Lett.*, 1988, 1571.
- H. Hiemstra and H. Wynberg, *Tetrahedron Lett.*, 1977, 2183.

‡ The optical yield compares favourably with stoichiometric additions using a monoalkyl zinc complex derived from the same ligand³ and with zincate additions using a chiral co-solvent.⁹