Pergamon

Tetrahedron Letters, Vol. 38, No. 10, pp. 1821-1824, 1997
© 1997 Published by Elsevier Science Ltd
All rights reserved. Printed in Great Britain.
0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00160-3

Dibutylboron Triflate Promoted Conjugate Addition of Benzylic and Allylic Organocopper Reagents to Chiral α,β-Unsaturated N-Acyl Imidazolidinones

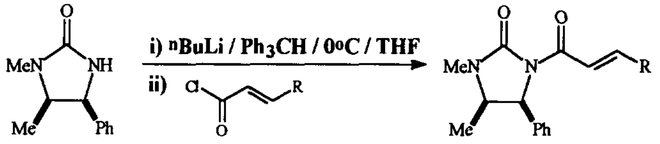
Pieter S. van Heerden,* Barend C.B. Bezuidenhoudt and Daneel Ferreira*

Department of Chemistry, University of the Orange Free State, P.O. Box 339, Bloemfontein, 9300 South Africa

Abstract. The organocopper-Lewis acid system, RCu-TMEDA-Bu_2BOTf, is useful for conjugate addition to highly constrained chiral α,β-unsaturated N-acyl imidazolidinones. In comparison with the corresponding TMSCl-activated reagents, Bu_2BOTf exhibits a dramatic increase in reactivity during 1,4-addition of benzylic and allylic organocopper reagents, which react more readily with crotonoyl-, and especially cinnamoyl imides.

The conjugate addition of organocopper-Lewis acid reagents to Michael acceptors is a highly useful reaction in selective organic synthesis.[1-8] Among the various Lewis acid systems that are available, Yamamoto's boron trifluoride based organocopper reagent ($RCu-BF_3$)[1] is, no doubt, the most widely used and versatile reagent. Besides promoting 1,4-addition to sterically highly crowded α,β-enones,[2] this Lewis acid system is reputed for effecting the transfer of alkyl and aryl ligands to unreactive α,β-unsaturated esters.[1] Surprisingly, however, attempts at transfering the highly reactive benzyl ligand to α,β-enoates using $BnCu-BF_3$ invariably failed.[9] Recently, excellent yields were recorded by utilization of the combined organocuprate-trimethylsilyl chloride reagent, BnCu-TMEDA-TMSCl, for benzyl transfer to a variety of α,β-enones and especially -enoates.[9,10] In order to extend this concept to asymmetric synthesis, we have undertaken a series of diastereoselective 1,4-addition reactions involving transfer of benzyl and allyl ligands to α,β-unsaturated N-acyl imidazolidinones. During the course of this study benzyl transfer to the corresponding cinnamoyl derivatives was hampered by excessive reaction times, hence initiating the development of a new organocopper-Lewis acid reagent, RCu-TMEDA-Bu_2BOTf. Here we wish to report the first examples of dibutylboron triflate[11,12] promoted conjugate addition of benzyl and allyl ligands to chiral α,β-unsaturated imides, affording β-alkylated N-acyl imidazolidinones in high yields and optical purity.

Owing to the excellent results obtained by Melnyk et al.,[13] the readily accessible (4S,5R)-(+)- **1** and (4R,5S)-(-)-1,5-dimethyl-4-phenyl-2-imidazolidinone **2** were chosen as chiral auxiliaries[14] for stereocontrol at the β-acyl position. Thus, the requisite conjugated imides **5**-**8** were synthesized in good yields (81-94%) *via* acylation of the lithium anions of **1** and **2** with either cinnamoyl chloride **3** or crotonoyl chloride **4** (Scheme 1).



1 (4S,5R)
2 (4R,5S)

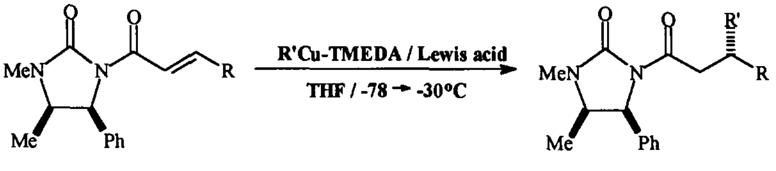
3 R=Ph
4 R=Me

5 (4R,5S), R=Ph, 93%
6 (4S,5R), R=Ph, 94%
7 (4R,5S), R=Me, 81%
8 (4S,5R), R=Me, 86%

Scheme 1

The organocopper derivatives were prepared by transmetalation between the CuI-TMEDA complex[15] and the corresponding Grignard reagents (prepared from magnesium and the appropriate alkyl chloride in THF), with subsequent addition of Bu_2BOTf or TMSCl at -78°C in THF. Table 1 summarizes the results of the Bu_2BOTf-activated cuprate addition of the benzyl and allyl ligands to chiral α,β-unsaturated imides **5**-**8**, in comparison with the classical TMSCl mediated addition reactions. The silyl based reagents exhibited good reactivity and led to complete conversion of all starting materials within 12 hours, the only exceptions being benzyl and *p*-methoxybenzyl transfer to the bulky cinnamoyl derivatives **5** and **6** (entries 2 and 7). However, despite the constraining steric and electronic effects, conjugate addition was readily facilitated through utilization of the corresponding boron-activated reagents, which provided imides **9** and **12** in slightly higher yields but within 10-12 hours (entries 1 and 6). In addition, further enhancement was observed during benzyl ligand transfer to the crotonoyl derivatives **7** and **8** (entries 4 and 8), while the corresponding allyl reagent also exhibited higher reactivity in reaction with imides **6** and **8** (entries 10 and 12). The Bu_2BOTf enhancement is presumably explicable in terms of boron acting as a much stronger chelating agent than TMSCl,[16,17] leading to a lowering in the LUMO energy of the substrate and hence promoting 1,4-addition.

With both Bu_2BOTf and TMSCl highly regio- (only 1,4-addition) and diastereoselective β-additions were observed. The diastereoisomeric ratios were determined by observing the doublet of the benzylic proton of the imidazolidinone moiety, which shows different chemical shifts in the ^1H NMR spectra of the two diastereomers.[13,18] The absolute configuration of N-acyl imidazolidinones **9** and **10** was assigned by hydrolysis of **9** and **10** and comparison of $[\alpha]_D$ values with those of the corresponding 3,4-diphenylbutyric acids,[19] while the absolute stereochemistry of adducts **14** and **15** was again assessed by comparison of optical rotations with those of authentic samples.[20] The absolute configurations are reconcilable in terms of preferential attack at the face of the double bond opposite to the phenyl and methyl groups of the imidazolidin-2-one moiety when the two carbonyls are considered to be complexed by the Lewis acid, and the acyl side chain is extended away from the chiral auxiliary (*s-trans* conformation) as was previously suggested.[21,22] The unambiguous determination of the absolute configurations of products **11-13** (entries 4-9) remain to be established. Assuming, however, that the stereochemistry of the reactions leading to those products is the same as for the previous entries (1-3, 10-13), it is reasonable to assume that adducts **11** and **12** correspond to the 3'S,4R,5S isomers and **13** to the 3'R,4S,5R isomer (Table 1).



5 - 8 **9 - 15**

Table 1. Conjugate Addition of Benzyl- and Allylorganocopper Reagents to N-Acyl Imidazolidinones 5-8

Entry	Substrate	R'	Lewis acid	Time (hours)	Product[a]	Yield (%)	de[b](%)
1	6	Bn	$^nBu_2BOTf$	12	9 R=Ph, R'=Bn	81	98 (R)
2	6	Bn	TMSCl	120	9 R=Ph, R'=Bn	75	99 (R)
3	5	Bn	$^nBu_2BOTf$	12	10 R=Ph, R'=Bn	84	96 (S)
4	7	Bn	$^nBu_2BOTf$	9	11 R=Me, R'=Bn	76	94 (S)
5	7	Bn	TMSCl	12	11 R=Me, R'=Bn	77	99 (S)
6	5	4-MeOBn	$^nBu_2BOTf$	10	12 R=Ph, R'=4-MeOBn	79	97 (S)
7	5	4-MeOBn	TMSCl	96	12 R=Ph, R'=4-MeOBn	77	99 (S)
8	8	4-MeOBn	$^nBu_2BOTf$	6	13 R=Me, R'=4-MeOBn	84	96 (R)
9	8	4-MeOBn	TMSCl	9	13 R=Me, R'=4-MeOBn	86	99 (R)
10	6	Allyl	$^nBu_2BOTf$	5	14 R=Ph, R'=Allyl	74	92 (R)
11	6	Allyl	TMSCl	10	14 R=Ph, R'=Allyl	80	99 (R)
12	8	Allyl	$^nBu_2BOTf$	5	15 R=Me, R'=Allyl	71	98 (R)
13	8	Allyl	TMSCl	10	15 R=Me, R'=Allyl	75	99 (R)

---

[a] All new compounds were fully characterized by spectroscopic methods, elemental composition being established by accurate mass measurement or microanalysis. [b] Absolute configuration at the β-carbon of the major product.

We have thus developed a new organocopper-Lewis acid system for the rapid and highly diastereoselective 1,4-addition of chiral imides. This methodology represents significant progress towards symmetric and asymmetric conjugate addition of sterically and electronically constrained Michael acceptors. The full potential and applications of this method are currently being investigated with a view to using the advantages offered by shortened reaction times.

Financial support by the Foundation for Research Development, Pretoria and by the 'Sentrale Navorsingsfonds' of this University is gratefully acknowlegded.

REFERENCES

1. Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.*, **1978**, *100*, 3240.
2. Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Ishihara, Y.; Maruyama, K. *J. Org. Chem.*, **1982**, *47*, 119.
3. Yamamoto, Y. *Angewandte Chemie*, **1986**, *25*, 947.
4. Smith, A.B., III; Jerris, P.J. *J. Am. Chem. Soc.*, **1981**, *103*, 194.
5. Ibuka, T; Minakata, H. *Synth. Commun.*, **1980**, *10*, 119.
6. Corey, E.J.; Boaz, N.W. *Tetrahedron Lett.*, **1985**, *26*, 6015, 6019.
7. a) Salomon, R.G. *Acc. Chem. Res.*, **1985**, *18*, 294; b) Salomon, R.G.; Miller, D.B.; Raychaudhuri, S.R.; Avasthi, K.; Lal, K.; Levison, B.S. *J. Am. Chem. Soc.*, **1984**, *106*, 8296.
8. Yamamoto, Y.; Yatagai, K.; Maruyama, *J. Org. Chem.*, **1979**, *44*, 1744.
9. Van Heerden, P.S.; Bezuidenhoudt, B.C.B.; Steenkamp, J.A.; Ferreira, D. *Tetrahedron Lett.*, **1992**, *33*, 2383.
10. Van Heerden, P.S.; Bezuidenhoudt, B.C.B.; Ferreira, D. *Tetrahedron*, **1996**, *52*, 12313.
11. Mukaiyama, T.; Inoue, T. *Chem. Lett.*, **1976**, 559.
12. Evans, D.A.; Nelson, J.V.; Vogel, E.; Taber, T.R. *J. Am. Chem. Soc.*, **1981**, *103*, 3099.
13. Melnyk, O.; Stephan, E.; Pourcelot, G.; Cresson, P. *Tetrahedron*, **1992**, *48*, 841.
14. Close, W.J. *J. Org. Chem.*, **1950**, *15*, 1131.
15. Johnson, C.R.; Marren, T.J. *Tetrahedron Lett.*, **1987**, *28*, 27.
16. Eriksson, M.; Johansson, A.; Nilsson, M.; Olsson, T. *J. Am. Chem. Soc.*, **1996**, *118*, 10904.
17. Lipshutz, B.H.; Aue, D.H.; James, B. *Tetrahedron Lett.*, **1996**, *37*, 8471.
18. Pourcelot, G.; Melnyk, O.; Besace, Y.; Stephan, E.; Cresson, P. *J. Organomet. Chem.*, **1990**, *388*, C5.
19. Chang, C.; Fang, J.; Liao, L. *J. Org. Chem.*, **1993**, *58*, 1754.
20. Bongini, A.; Cardillo, G.; Mingardi, A.; Tomasini, C. *Tetrahedron: Asymmetry*, **1996**, *7*, 1457.
21. Oppolzer, W.; Mills, R.J.; Rachinger, W.; Stevenson, T. *Helv. Chim. Acta*, **1986**, *69*, 1542.
22. Bergdahl, M.; Nilsson, M.; Olsson, T.; Stern, K. *Tetrahedron*, **1991**, *47*, 9691.

(*Received in UK* 11 *December* 1996; *revised* 20 *January* 1997; *accepted* 24 *January* 1997)