An improved vinylalumination procedure replacing HMPA with NMO for the hydroalumination of α-acetylenic esters and ketones

P. Veeraraghavan Ramachandran,* M. Venkat Ram Reddy and Michael T. Rudd

H. C. Brown and R. B. Wetherill Laboratories of Chemistry, Purdue University, West Lafayette, Indiana 47907-1393, USA. E-mail: chandran@purdue.edu

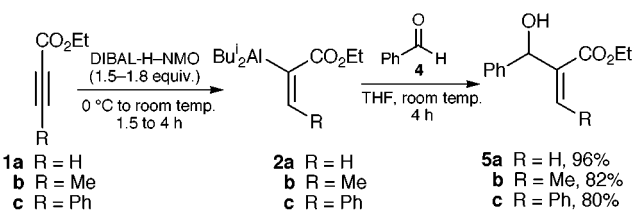
Received (in Corvallis, OR, USA) 15th July 1999, Accepted 20th August 1999

Replacing carcinogenic HMPA with NMO, a higher yielding, enviornmentally benign procedure for the vinylalumination of carbonyl compounds with [α-(ethoxycarbonyl)-vinyl]diisobutylaluminium and its β-methyl or -phenyl analogs, as well as [α-(acetyl)vinyl]diisobutylaluminium has been developed.

Vinylalumination,[1] a carbon–carbon bond forming reaction of vinylaluminium derivatives with electrophiles, provides Morita–Baylis–Hillman[2] type products without the reaction's limitations. For example, (i) the electrophiles are not limited to reactive carbonyls and imines, (ii) the reaction times are considerably shorter, and (iii) β-substitution of the vinyl moiety is readily accommodated.

Although known for over a decade, the lack of extensive utilization of this potentially useful reaction may be due to the presence of a carcinogenic material, HMPA,[3] as the complexing agent with DIBAL-H for the hydroalumination of propiolates. Several possible replacements for HMPA, such as 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DMPU),[4a] 1,3-dimethylimidazolidin-2-one (DMEU or DMI),[4b] and quinuclidine *N*-oxide (QNO)[4c] have been reported in the literature. Since DMPU and DMI might undergo reduction with DIBAL-H and QNO is not economical, we studied a series of other amine oxides as complexing agents. Although mixtures of DIBAL-H and aromatic amine oxides, such as pyridine and picoline *N*-oxides, did not provide the required hydroalumination product, aliphatic trialkylamine oxides, such as trimethylamine *N*-oxide and NMO, were found to be suitable complexing agents for the hydroalumination of propargylic esters and ketones. Our study with the relatively inexpensive NMO revealed it to be an excellent HMPA alternative for vinylaluminations, improving the reaction conditions and providing superior yields of the products. We also noticed that Lewis acid catalysis[1d] and low reaction temperatures[1d] are not essential for reactions with the β-methyl and -phenyl substituted reagents.

The addition of DIBAL-H to a suspension of NMO in THF provided a clear solution. The reaction of ethyl propiolate **1a** in THF with 1.5 equiv. DIBAL-H–NMO in hexanes at 0 °C provided the [α-(ethoxycarbonyl)vinyl]diisobutylaluminium **2a**. Benzaldehyde **4** (1.2 equiv.) was added to this reagent at 0 °C and warmed to room temperature. The reaction was complete within 4 h. Hydrolysis using 1.0 *M* HCl, followed by chromatography, provided 96% yield of the product **5a** (Scheme 1). Earlier procedures employing HMPA utilized 2 equiv. of the aldehyde.[1] We observed that the hydrolysis was much more facile when compared to the reactions using HMPA.[1] The reaction provided high yields of the products with all of the aldehydes, *viz.* butyraldehyde **6**, isobutyraldehyde **8**, pivalaldehyde **10** and fluoral **12**.



Scheme 1

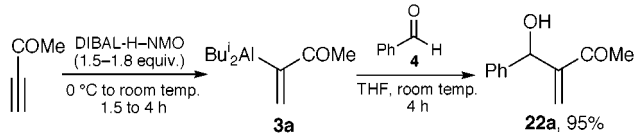
The corresponding β-substituted vinylaluminium reagent, [α-(ethoxycarbonyl)-β-methylvinyl]diisobutylaluminium **2b**, reacted with **4** smoothly to provide ethyl (*Z*)-1-hydroxy-1-phenylbut-2-enoate **5b** in 82% yield (Scheme 1). The β-phenylvinyldiisobutylaluminium reagent **2c** yielded 80% of the corresponding *Z* product **5c**. The stereochemistry of the alkenes (^{1}H NMR) is exclusively *Z*.[1e] In contrast to the earlier reported procedure involving HMPA,[1d] neither of these reactions require Lewis acid catalysis or low temperatures (−78 °C).

The reaction of acetophenone **14** with **2a** was sluggish. We worked up the reaction after 2 d and obtained only 12% yield of the product **15a** along with 25% of recovered **14** and a mixture of unidentified products. Addition of 10% of a Lewis acid, such as $BF_3{\cdot}Et_2O$, provided a small amount of the product with most of the ketone recovered. Upon the addition of 1 equiv. of $BF_3{\cdot}Et_2O$, the reaction was complete within 4 h, and work up provided a 74% yield of **15a** (Table 1, entry 12). Butan-2-one **16** reacted similarly, in the presence of 1 equiv. of $BF_3{\cdot}Et_2O$, providing the product in 75% yield (Table 1, entry 15). Reagents **2b** and **2c** gave similar results with these ketones.

An activated ketone, such as 2,2,2-trifluoroacetophenone **18**, reacted similar to an aldehyde, without Lewis acid, and the product **19a** was obtained in 95% yield (Table 1, entry 18). We then examined the reaction of **2a** with ethyl pyruvate **20**, and obtained the corresponding product alcohol in 95% yield (Table 1, entry 19).

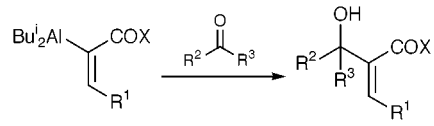
The procedure was then extended to α-acetylvinyldiisobutylaluminium **3a**, prepared *via* the hydroalumination of but-3-yn-2-one with DIBAL-H–NMO complex (Scheme 2). A 23–31% yield of products from benzaldehyde and butyraldehyde for a reaction of **3a** prepared with DIBAL-H–HMPA was reported by Tsuda.[1a] Replacement of HMPA with NMO provided a 36% yield of **22a**. However, utilization of 2 equiv. of the reagent improved the yield to 95% (Scheme 2). We used these modified conditions for the reaction of the same series of aldehydes (**4**, **6**, **8**, **10**, **12**) with **3a** and the products were obtained in 72–95% yield. However, ketones did not react with **3a**. All of the results are summarized in Table 1.

In conclusion, we have described a significantly improved procedure for the vinylalumination of a variety of carbonyl compounds with [α-(ethoxycarbonyl)vinyl]- and (α-acetylvinyl)diisobutylaluminium. Replacement of carcinogenic HMPA with readily available NMO in the hydroalumination step makes this procedure environmentally benign. The work up is simpler and the yields of the products are considerably higher in most cases. We have also shown that Lewis acid catalysis and low reaction temperatures are not essential for reactions with



Scheme 2

Table 1 Vinylalumination of aldehydes and ketones[a]



	Reagent			R^2COR^3			Product	
Entry	No.	R^1	X	No.	R^2	R^3	No.	Yield[b] (%)
1	**2a**	H	OEt	**4**	Ph	H	**5a**	96 (83)[a]
2	**2b**	Me	OEt	**4**	Ph	H	**5b**	82 (58)[d]
3	**2c**	Ph	OEt	**4**	Ph	H	**5c**	80 (61)[d]
4	**2a**	H	OEt	**6**	Pr	H	**7a**	90
5	**2b**	Me	OEt	**6**	Pr	H	**7b**	90
6	**2c**	Ph	OEt	**6**	Pr	H	**7c**	75
7	**2a**	H	OEt	**8**	Pr^i	H	**9a**	88
8	**2a**	H	OEt	**10**	Bu^t	H	**11a**	72
9	**2a**	H	OEt	**12**	CF_3	H	**13a**	80
10	**2b**	Me	OEt	**12**	CF_3	H	**13b**	70
11	**2c**	Ph	OEt	**12**	CF_3	H	**13c**	75
12	**2a**	H	OEt	**14**[e]	Ph	Me	**15a**	74
13	**2b**	Me	OEt	**14**[e]	Ph	Me	**15b**	72
14	**2c**	Ph	OEt	**14**[e]	Ph	Me	**15c**	70
15	**2a**	H	OEt	**16**[e]	Et	Me	**17a**	75
16	**2b**	Me	OEt	**16**[e]	Et	Me	**17b**	80
17	**2c**	Ph	OEt	**16**[e]	Et	Me	**17c**	70
18	**2a**	H	OEt	**18**	Ph	CF_3	**19a**	95 (70)[f]
19	**2a**	H	OEt	**20**	Me	CO_2Et	**21a**	95 (65)[g]
20	**3a**	H	Me	**4**[h]	Ph	H	**22a**	95
21	**3a**	H	Me	**6**[h]	Pr	H	**23a**	72
22	**3a**	H	Me	**8**[h]	Pr^i	H	**24a**	80
23	**3a**	H	Me	**10**[h]	Bu^t	H	**25a**	80
24	**3a**	H	Me	**12**[h]	CF_3	H	**26a**	84

[a] The reactions were carried out in THF at room temperature with 1.2 equiv. of the carbonylcompound. [b] All of the yields are of isolated, purified products. Values in parenthesis are from a reaction with the reagent made using DIBAL-H–HMPA. [c] Ref. 1(*a*). [d] Ref. 1(*d*). [e] 1 equiv. of BF_3•Et_2O was added. [f] Ref. 1(*e*). [g] Ref. 1(*f*). [h] 2 equiv. of reagent was essential for complete reaction.

the β-methyl and -phenyl substituted reagents. Further explorations and a study of the mechansim of this reaction are in progress.

Financial assistance from the Purdue Borane Research Fund is gratefully acknowledged.

Notes and references

1 (*a*) T. Tsuda, T. Yoshida and T. Saegusa, *J. Org. Chem.*, 1988, **53**, 1037; (*b*) Y. Génisson, C. Massardier, I. Gautier-Luneau and A. E. Greene, *J. Chem. Soc., Perkin Trans. 1*, 1996, 2869; (*c*) L. H. Zu and E. P. Kundig, *Helv. Chim. Acta*, 1994, **77**, 1480; (*d*) G. Li, H. X. Wei and S. Willis, *Tetrahedron Lett.*, 1998, **39**, 4607; (*e*) P. V. Ramachandran, M. V. R. Reddy, M. T. Rudd and J. R. de Alaniz, *Tetrahedron Lett.*, 1998, **39**, 8791; (*f*) P. V. Ramachandran, M. V. R. Reddy and M. T. Rudd, *Tetrahedron Lett.*, 1999, **40**, 627.

2 For the most recent review of the Morita–Baylis–Hillman reaction, see: E. Ciganek, *Org. React.*, 1997, **51**, 201.

3 J. F. Schmutz, *Chem. Eng. News*, 1978, **56 (3)**, 39; H. Spencer, *Chem. Ind.*, 1979, 728.

4 (*a*) T. Mukhopadhyay and D. Seebach, *Helv. Chim. Acta*, 1982, **65**, 385; (*b*) E. Juaristi, P. Murer and D. Seebach, *Synthesis*, 1993, 1243; (*c*) I. A. O'Neil, J. Y. Q. Lai and D. Wynn, *Chem. Commun.*, 1999, 56.

Communication 9/05836B