Tetrahedron Letters, Vol.27, No.8, pp 933-934, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

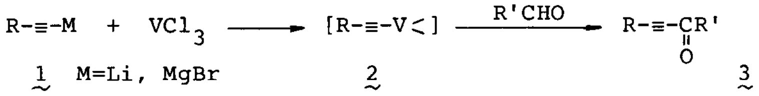
VERSATILE SYNTHESIS OF α,β-ACETYLENIC KETONES BY OXIDATIVE NUCLEOPHILIC ADDITION OF VANADIUM ACETYLIDES

Toshikazu Hirao,* Daisuke Misu, and Toshio Agawa
Department of Applied Chemistry, Faculty of Engineering, Osaka University,
2-1 Yamadaoka, Suita, Osaka 565, Japan

Summary: Treatment of aldehydes with vanadium acetylides generated from equimolar amounts of vanadium trichloride and acetylenic Grignard or lithium compounds gave α,β-acetylenic ketones via oxidative nucleophilic addition.

A previous paper[1] disclosed the novel reactions of organovanadium compounds, affording a conceptually new methodology for carbonyl alkylation, oxidative nucleophilic addition. Organic moiety of nucleophilic organo-transition metal compounds is generally limited to alkyl, vinyl, or aryl group. The corresponding acetylides show the lower reactivity and have not sufficiently been investigated.[2] We now report that the oxidative nucleophilic addition reaction is applicable to vanadium acetylides providing a general and useful method for α,β-acetylenic ketone syntheses.

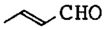
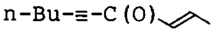
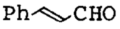
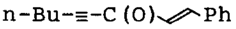
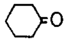
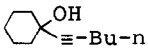
The vanadium acetylides 2 were generated in CH_2Cl_2 at -78 °C by simple treatment of vanadium trichloride with 1 equiv of acetylenic Grignard or lithium compounds (1). The reagents 2 easily reacted with aldehydes leading to the corresponding α,β-acetylenic ketones 3 in good or moderate yields;[3] the conversion yields were almost quantitative (Table I). The oxidation process proceeded smoothly even at the refluxing temperature of CH_2Cl_2, it being much lower as compared to the reaction with alkenyl- or arylvanadium compounds. Except this finding, the surprising analogy in reactivities was observed. For the successful transformation of alkyl aldehydes, the reagents 2 from acetylenic Grignard compounds should be employed although the reason has not been clarified. Use of a lithium acetylide instead gave the alcohol exclusively.



$$\underset{\mathbf{1}\ \ M=Li,\ MgBr}{R-\equiv-M} + VCl_3 \longrightarrow \underset{\mathbf{2}}{[R-\equiv-V<]} \xrightarrow{R'CHO} \underset{\mathbf{3}}{R-\equiv-\underset{\overset{\|}{O}}{C}R'}$$

The high regioselectivity and chemoselectivity raise the synthetic utility

Table I. The reaction of 2 with Carbonyl Compounds

R-≡-M for 2		R'CHO	Refluxing Time, h	Yield, %[a]		
n-Bu-≡-Li	1a	PhCHO	5	n-Bu-≡-C(O)Ph 3a	71	(60)
1a		p-Cl-C_6H_4CHO	10	n-Bu-≡-C(O)C_6H_4-Cl-p	45	
1a		p-NC-C_6H_4CHO	10	n-Bu-≡-C(O)C_6H_4-CN-p	54	
1a			4		50	
1a			4		51	
1a		n-PrCHO	15	n-Bu-≡-CH(OH)Pr-n	64	
1a			-		62	
n-Oct-≡-Li	1b	PhCHO	5	n-Oct-≡-C(O)Ph	62	(51)
Ph-≡-Li	1c	PhCHO	5	Ph-≡-C(O)Ph	66	(54)
n-Bu-≡-MgBr	1d	n-PrCHO	5	n-Bu-≡-C(O)Pr-n	63	
1d		n-HepCHO	5	n-Bu-≡-C(O)Hep-n	61	
n-Oct-≡-MgBr	1e	n-PrCHO	5	n-Oct-≡-C(O)Pr-n	60	
Ph-≡-MgBr	1f	n-PrCHO	5	Ph-≡-C(O)Pr-n	51	

a) Yields were determined by NMR. Isolated yields are shown in parentheses.

of vanadium acetylides. α,β-Unsaturated aldehydes underwent regioselective 1,2-addition leading to the corresponding 1-en-4-yn-3-ones. Aldehydes can be distinguishable from ketones with high selectivity although ketone was reactive enough towards the organovanadium compound. The reaction of 2a with a 1:1 mixture of benzaldehyde and acetophenone exclusively gave the ketone 3a derived from benzaldehyde (46%). The presence of chloro or cyano functionality on phenyl ring did not interfere with nucleophilic addition to aldehydes.

Dichlorovanadium acetylides are assumed to be active species which undergo nucleophilic addition to aldehydes, followed by oxidation of the vanadium sec-alkoxide intermediates. The α,β-acetylenic ketones were selectively converted to (Z)-α,β-unsaturated ketones in excellent yields by hydrogenation with Pd/$BaSO_4$-quinoline (e. g., 93% from 3a). Further investigation is in progress.

References

1. T. Hirao, D. Misu, and T. Agawa, J. Am. Chem. Soc., in press.
2. For example, T. F. Rutledge, "Acetylenic Compounds", Reinhold Book Corporation, 1968.
3. The general procedure is as follows. The conversion of terminal acetylenes to 1 was done by treatment with n-BuLi in CH_2Cl_2 at -78 °C or with n-BuMgBr in Et_2O at 0 °C. Since use of Et_2O as solvent greatly decreased the yields of 3, the concentration of ethereal Grignard reagent should be as high as possible. Thus obtained acetylide 2 was dropwise added to a suspension of VCl_3 (1 equiv) in CH_2Cl_2 at -78 °C. The mixture was kept at -78 °C for 20 min with stirring and then an aldehyde (1 equiv) was added. Stirring was continued at -78 °C for 2 h. The mixture was warmed to room temperature and heated at reflux. Workup with saturated $NaHCO_3$ solution and column chromatography gave 3.

(Received in Japan 1 October 1985)