Tetrahedron Letters, Vol.27, No.8, pp 929-932, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

HIGHLY CHEMOSELECTIVE COUPLING REACTIONS OF ORGANOVANADIUM COMPOUNDS

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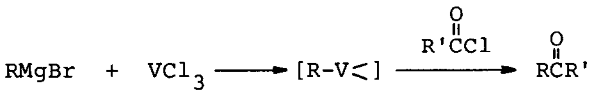
Summary: Organovanadium compounds generated in dichloromethane from equimolar amounts of vanadium trichloride and Grignard reagents underwent the chemoselective cross-coupling reaction with acid chlorides leading to the corresponding ketones. Treatment with allyl halides resulted in allylation of organovanadium compounds. In the case of propargyl bromide, regioselective displacement occurred to produce allene derivatives.

A variety of organometallic reagents have been developed to achieve selective carbon-carbon bond construction.[1,2] In a previous paper,[3] organovanadium compounds were revealed to be novel reagents with synthetic potential, allowing a facile, direct synthesis of ketones from aldehydes via oxidative nucleophilic addition. The finding of this new methodology prompted us to investigate another efficient route for carbon-carbon bond formation with organovanadium reagents. We now describe highly selective coupling reactions with organic halides.

Using organovanadium reagents generated in situ in dichloromethane from equimolar amounts of vanadium trichloride and Grignard reagents, chemoselective coupling with a wide variety of acid chlorides was performed to give the corresponding ketones (Table I).[4] To get a higher yield of ketone, dichloromethane was superior to ether as solvent. It should be noted that loss of chloride or bromide α to acid chlorides was not observed giving α-haloketones exclusively. Furthermore, bromine atom of p-bromobenzoyl chloride was not displaced by the organovanadium reagent. Although organovanadium compounds are nucleophilic enough towards ketones,[3] the oxo group was left intact by their



$$\mathrm{RMgBr} + \mathrm{VCl_3} \longrightarrow [\mathrm{R{-}V}<] \xrightarrow{\mathrm{R'}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{Cl}} \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{R'}$$

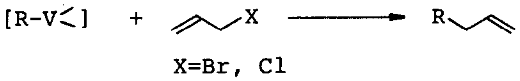
attack. The presence of ester or nitrile functionality did not interfere with the coupling reaction. Additionally, ketones capable of enolization were also produced without condensation. These characteristics indicate that the organovanadium reagents indeed engage in this transformation.

Table I. Preparation of Ketones from Acid Chlorides

RMgBr for RV<	R'C(O)Cl	RC(O)R'	Yield, %
R=Ph	R'=o-MeC_6H_4	$\mathrm{Ph\overset{O}{\overset{\|}{C}}C_6H_4Me\text{-}o}$	86 53^{a}
n-Bu[b]	o-MeC_6H_4	$\mathrm{n\text{-}Bu\overset{O}{\overset{\|}{C}}C_6H_4Me\text{-}o}$	86
Ph	p-$N{\equiv}CC_6H_4$	$\mathrm{Ph\overset{O}{\overset{\|}{C}}C_6H_4C{\equiv}N\text{-}p}$	83
Ph	p-BrC_6H_4	$\mathrm{Ph\overset{O}{\overset{\|}{C}}C_6H_4Br\text{-}p}$	70
Ph[b]	Me	$\mathrm{Ph\overset{O}{\overset{\|}{C}}Me}$	89
Ph[b]	$EtOOC(CH_2)_4$	$\mathrm{Ph\overset{O}{\overset{\|}{C}}(CH_2)_4COOEt}$	76
Ph[b]	$\mathrm{Me\overset{O}{\overset{\|}{C}}(CH_2)_2}$	$\mathrm{Ph\overset{O}{\overset{\|}{C}}(CH_2)_2\overset{O}{\overset{\|}{C}}Me}$	81
n-Bu[b]	$\mathrm{Me\overset{O}{\overset{\|}{C}}(CH_2)_2}$	$\mathrm{n\text{-}Bu\overset{O}{\overset{\|}{C}}(CH_2)_2\overset{O}{\overset{\|}{C}}Me}$	78
Ph[b]	$ClCH_2$	$\mathrm{Ph\overset{O}{\overset{\|}{C}}CH_2Cl}$	61
Ph[b]	Cl_2CH	$\mathrm{Ph\overset{O}{\overset{\|}{C}}CHCl_2}$	89
Ph[b]	EtCH(Br)	$\mathrm{Ph\overset{O}{\overset{\|}{C}}CH(Br)Et}$	72

a) Solvent, ether. b) The reaction was carried out by adding the organovanadium species into a solution of acid chloride.

Allyl bromide worked as an efficient electrophile for coupling reactions. Dichloromethane was also a preferable solvent. However, with butyl bromide, butyl iodide, and β-bromostyrene, no cross-coupled products were obtained even at elevated reaction temperature (-10 °C). Using allyl chloride, allylation of the generated phenylvanadium species proceeded well. The other halides rather



than allyl halides (Table II) were very poor reaction partners or did not react at all under the conditions employed here only leading to a small amount of homo-coupled compounds derived from organovanadium species. These results allowed the selective formation of allylbenzene in the competition reaction of phenylvanadium species with a mixture of allyl bromide and benzyl bromide. The feature is much more distinct as compared with the reactions of usual organo-

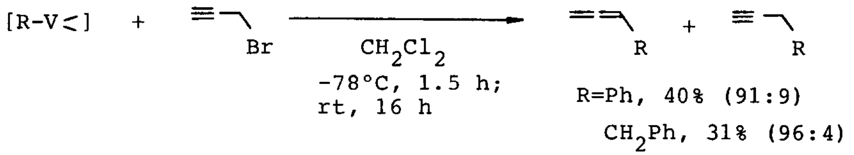
Table II. Reaction of Organovanadium Compounds with Organic Halides[a]

RMgBr for RV<	R'X	Time, h	R-R'	Yield, %
R=Ph	CH_2=$CHCH_2Br$	2.5	$PhCH_2CH$=CH_2	93
		18[b]		43
		18[c]		32
	CH_2=$CHCH_2Cl$	14	$PhCH_2CH$=CH_2	70
	n-BuBr	23	-	0
	n-BuI	20[d]	-	0
	$PhCH_2Br$	2.5	-	0
	PhCH=CHBr	18	-	0
	CH_2=$CHCH_2Br$[e] $PhCH_2Br$[e]	20	$PhCH_2CH$=CH_2	30[f]
CH_2Ph	CH_2=$CHCH_2Br$	16.5	$PhCH_2CH_2CH$=CH_2	57
	n-BuBr	16.5	-	0
CH_2CH=CH_2	PhBr	19	-	0
	$PhCH_2Br$	19	$PhCH_2CH_2CH$=CH_2	14
CH=CHPh	CH_2=$CHCH_2Br$	18	$PhCH$=$CHCH_2CH$=CH_2	58
Oct-n	CH_2=$CHCH_2Br$	24	n-$OctCH_2CH$=CH_2	45

a) R'X (1 equiv) was added to a mixture of the organovanadium species in dichloromethane at -78 °C and stirring continued at the same temperature for 1.5 h. The resultant mixture was warmed up to room temperature and stirred for the time shown in Table II. b) Solvent, ether. c) Solvent, THF. d) The reaction was carried out at -10 °C for 1.5 h after the addition of n-BuI at -78 °C. Then stirring continued at room temperature. e) 0.5 equiv. f) Yield was based on PhMgBr. The formation of diphenylmethane was not observed.

metallic reagents.[2] Since a combination of bromobenzene or benzyl bromide with the vanadium species pre-generated from allylmagnesium bromide led to no or a small amount of cross-coupled product, the coupling reaction is assumed to proceed by the direct attack of the organovanadium species to allyl bromide.

Based on regioselective substitution with organovanadium compounds, propargyl bromide was converted to allene derivatives predominantly although the yields were not high.



The detailed reaction mechanism has not been elucidated yet, but a reagent participating in coupling reactions is presumed to be $RVCl_2$ as proposed previously.[3] The carbon-carbon bond-forming reaction via organovanadium reagents lies in its usefulness for organic synthesis.[5]

References and Note

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4. A typical procedure is as follows. A Grignard reagent (1.0 mmol) was added to a suspension of vanadium trichloride (1.0 mmol) in dichloromethane (2 mL) at -78 °C over 10 min. After further stirring for 20 min, acid chloride (1.0 mmol) was added to the resultant mixture at -78 °C, which was kept at the same temperature for 1.5 h. The mixture was warmed to room temperature and stirred for 16 h. Workup with saturated $NaHCO_3$ solution and column chromatography gave the desired ketone.
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(Received in Japan 12 December 1985)