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REACTIONS OF ORGANIC HALIDES WITH OLEFINS UNDER Ni^0-CATALYSIS. FORMAL ADDITION OF HYDROCARBONS TO CC-DOUBLE BONDS

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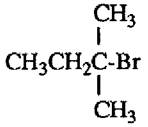
The reaction of various types of organic halides with electron deficient olefins under the influence of $NiCl_2$ x 6 H_2O in the presence of zinc and pyridine leads to formal addition products of hydrocarbons to CC-double bonds in good yield.

The competition of reductive elimination and β-hydrogen elimination plays often a decisive role for the applicability and scope of possible organometallic reactions in organic synthesis. In an attempt to gain more insight in these processes and their interrelationship we studied their competition in related complexes[1,2]. These results led us to an application of bipyridine(olefin)palladium(0) complexes as precatalysts in CC-couplings of organohalogen compounds with tin-organic compounds [3], a reaction which has been studied extensively by Stille using organopalladium catalysts with phosphane ligands [4]. Noteworthy in our investigation is the possibility to influence the competition of CC-coupling and β-hydrogen elimination in favor of the CC-bond formation by addition of electron deficient olefins. Thus α-phenylethyl bromide can be coupled with tetramethyl tin to cumene in the presence of bipyridine(fumaronitrile)palladium(0) [3]. The transfer of these results from palladium to nickel as transition metal failed so far [5]. However, in the course of these studies we discovered the possibility to obtain formal addition products of hydrocarbons to olefins in high yield by reacting organic halides with olefins in the presence of $NiCl_2$ x $6H_2O$, Zn and pyridine. This is formulated in equation 1 for ethyl acrylate as olefin.

$$R\text{-}X \;+\; H_2C{=}CHCO_2C_2H_5 \xrightarrow[\text{THF, Zn, pyridine}]{NiCl_2 \text{ x } 6\,H_2O} RCH_2CH_2CO_2C_2H_5 \qquad \text{eq.1}$$

Table 1 shows results for the reaction of ethyl acrylate with a variety of organic halides and Table 2 displays results for the reaction of cis-1-bromo-1-propene with different olefins. The reactions are carried out on a ca. 20-30 mmol scale either with the olefin as solvent or in tetrahydrofuran using the following molar ratios: R-X : olefin : Zn : pyridine = 1 : 1.9 : 2.3 :1.4. These were optimized for the reaction of cis-1-bromo-1-propene and ethyl acrylate and applied in similar fashion to the other examples. $NiCl_2$ x $6H_2O$ is used in general in ca. 15-20 molar percent relative to the organic halide (see below). The reactions are carried out at 60°C in such a way that a suspension of zinc [6] in THF is stirred with nickel(II)chloride in the presence of the olefin for 15 min before the alkylhalide is added. In some cases (aliphatic halides) it is advisable to add the organic halide over a period of ca. 20 min. in order to increase the yield. The reaction is assumed to proceed as follows: Ni^{2+} is reduced by Zn to Ni^0 which is stabilized by complexation to the olefin and pyridine. In the absence of pyridine the desired reaction does not take place. Oxidative addition of RX to Ni^0 gives a new organometallic complex. Insertion of olefin and subsequent hydrolysis gives the reaction product. Zn has to be used in more than stoichiometric amounts because it not only forms $ZnCl_2$ but also is involved in the final hydrolysis step. We assume that it binds hydroxide ion after a proton of a water molecule has hydrolyzed a nickel-carbon bond. The amount of pyridine takes into consideration that it is complexed to $ZnCl_2$. The products are isolated after separation from the metal salts by distillation. No products of substitution (Heck reaction) are formed.

Table 1: Products of conjugate addition of organyl halides to ethyl acrylate .

organyl halide	product[a)]	time(h)	yield(%)[b)]	Ref.
$H_3C\text{-}(CH_2)_6\text{-}CH_2Br$	$H_3C\text{-}(CH_2)_9CO_2C_2H_5$	200	69(75)	7
$c\text{-}C_6H_{11}Br$	$c\text{-}C_6H_{11}CH_2CH_2CO_2C_2H_5$	72	65(73)	8
 $CH_3CH_2C(CH_3)_2Br$	$H_3CCH_2C(CH_3)_2CH_2CH_2CO_2C_2H_5$	48	79(77)	9
C_6H_5J	$C_6H_5CH_2CH_2CO_2C_2H_5$	48	72(92)	7
cis-$C_6H_5CH{=}CHBr$	cis-$C_6H_5CH{=}CHCH_2CH_2CO_2C_2H_5$	4	75(80)	10
trans-$C_6H_5CH{=}CHBr$	trans-$C_6H_5CH{=}CHCH_2CH_2CO_2C_2H_5$	4	72(80)	11
cis-$H_3CCH{=}CHBr$	cis-$CH_3CH{=}CHCH_2CH_2CO_2C_2H_5$	4	70(96)	12

a)all new products were characterized by spectroscopic means and gave satisfactory elemental analyses; b)yields in brackets by GLC after 20 h.

Several points are remarkable: A variety of different organic halides can be used in this reaction ranging from aromatic and vinylic to saturated aliphatic halides. In contrast to many other organometallic reactions with organic halides we can use primary, secondary and tertiary halides which have hydrogen atoms in β-position to the leaving group at a sp^3-hybridized carbon atom. This opportunity widens the scope of application drastically and provides, for example with methyl acrylate as substrate, a general synthesis of carboxylic acid esters. From our studies on the reductive elimination from diethyl(bipyridine)palladium(II) in the presence of electron deficient olefins it seems logical to assume that it is a molecule of α,β-unsaturated ester complexed to nickel which hinders β-elimination after oxidative addition of the alkyl halide. Furthermore, the reaction seems to be highly stereoselective if not stereospecific. With cis and trans β-bromostyrene and ethyl acrylate two different products are formed in greater than 99% stereoselectivity. According to the ^{1}H-NMR data the reactions occur with retention of configuration at the double bond. Thus the product of reaction with cis-β-bromostyrene displays a vicinal coupling of 11.8 Hz for the olefinic protons and an IR band at 710 cm^{-1}, while the compound isolated from the reaction of trans-β-bromostyrene shows a coupling of 15.7 Hz for these protons and an IR band at 975 cm^{-1}. The degree of specificity of the reaction was checked by GLC and ^{1}H-NMR spectroscopy.

Table 2: Products of conjugate addition of cis-1-bromo-1-propene

olefin	product	yield(%)	Ref.
$H_2C=CHCO_2C_2H_5$	cis- $H_3CCH=CHCH_2CH_2CO_2C_2H_5$	70	12
$H_2C=CH\text{-}CN$	cis- $H_3CCH=CHCH_2CH_2CN$	66	13
$H_2C=CH\text{-}COCH_3$	cis- $H_3CCH=CHCH_2CH_2COCH_3$	58	14

So far electron deficient olefins give the best results. Besides ethyl acrylate and acrylonitrile we tested methyl vinylketone (Table 2). The possibility of the olefin to complex with Ni^0 under our conditions might be the limiting factor in the application. Further studies as to the scope of application are in progress. Entries 1 and 3 of table 2 are related to pheromones [12,15] and were synthesized earlier [12,14] by other procedures.

The amount of water present in the system is decisive for the turnover number which can be obtained with $NiCl_2$. If anhydrous nickel(II)chloride is used the turnover numbers do not surpass 2 or 3. It seems as if residual water in the solvent or reactants, even though they were thoroughly dried, provide the necessary protons for hydrolysis of a nickel carbon bond. By adding water externally in varying amounts it was possible to increase the turnover numbers up to the expected value. So far we have reached turnover numbers of ca. 20 which probably do not constitute the limit. Under preparative conditions we use presently 15 molar percent of $NiCl_2 \times 6H_2O$ because this does not require an extra addition of water. It has been shown also that addition of deuterium oxide leads to the incorporation of deuterium in α-position of the substituent in the olefin.

Pyridine is not the only base which can effect this reaction. The reaction of cis-1-bromo-1-propene with ethyl acrylate in the olefin as solvent was also carried out with α-picoline, 2,4-lutidine, N-methylimidazole, 2-methyloxazoline and 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU). Unsuccessfully tested were 2,4,6-collidine, pyrimidine and tetramethylethylenediamine (TMEDA).

The reaction of the couple $NiCl_2$/Zn with organic halides and olefins has been studied in the presence of two equivalents of triphenylphosphane [16]. With styrene and aryliodides biphenyl formation and substitution products (Heck reaction) were observed in this case. With ethyl acrylate and aryl- or vinylhalides small amounts of the product of conjugate addition besides Heck type products were obtained. Lebedev et al. [8] studied the catalytic system $(Ph_3P)_2NiCl_2$/Zn/Pyridine in detail. Styrene and aryl iodides yield Heck type products, methyl acrylate leads as in our case to products of conjugate addition. They realize that pyridine and water are necessary but do not elaborate on the role of pyridine. In the light of our results it seems questionable whether triphenylphosphane has to be present. Indeed, the conjugate addition can be carried out without competition with other reactions under our conditions much better and cleaner. The comparison with the Heck reaction [17,18] is of interest where a vinylic hydrogen of the olefin is substituted by the organic residue of the halide. These reactions are performed with phospane complexes of palladium as catalysts in the presence of a tertiary amine. It is noteworthy that in this reaction aliphatic halides with a sp^3 bonded hydrogen atom β to the halide can not be reacted.

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9. ^{1}H NMR ($CDCl_3$): δ= 0.82(t,J=7.3Hz,3H), 0.84(s,6H), 1.23(q,J=7.3Hz,2H), 1.26(t,J=7 .3,2H), 2.24(m,2H), 4.12(q,J=7.3Hz); ^{13}C NMR($CDCl_3$): δ=13.68(q), 25.73(q), 29.06(t), 31.88(s), 33.44(t), 35.56(t), 59.47(t), 173.41(s). BP 102°C/35 Torr.
10. ^{1}H NMR ($CDCl_3$): δ= 1.22(t,J=7.1Hz,3H), 2.42(t,J=7.3Hz,2H), 2.63(m,2H), 4.11(q,J=7.15Hz), 5.63(dt,J=11.8 and 7.15Hz,1H), 6.47(d,J=11.8Hz,1H), 7.29(m,5H,C_6H_5); ^{13}C NMR ($CDCl_3$): δ= 14.16(q), 24.01(t), 34.37(t), 60.33(t), 125.82(d), 126.87(d), 127.97(d), 128.24(d), 130.70(d), 137.15(s), 172.90(s), BP 130-140°C/16 Torr.
11. ^{1}H NMR ($CDCl_3$): δ= 1.22(t,J=7.15Hz,3H), 2.46(m,4H), 4.11(q,J=7.15Hz,2H), 6.17(dt,J=15.7 and 6.3Hz,1H), 6.41(d,J=15.7Hz,1H), 7.28(m,5H,C_6H_5). ^{13}C NMR ($CDCl_3$): δ= 14.03(q), 28.06(t), 33.75(t), 60.06(t), 126.68(d), 128.16(d), 128.64(d), 130.06(d), 130.30(d), 137.15(s), 172.55(s). BP 85-87°C/0.5 Torr.
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