

Condensation of organic bromides with vinyl compounds catalysed by nickel complexes in the presence of zinc

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Abstract

The catalytic system $(\text{Ph}_3\text{P})_2\text{NiCl}_2$ /zinc/pyridine in acetonitrile is an effective catalyst for reactions of aryl and alkyl bromides with styrene and methyl acrylate. With styrene, the reaction yields vinyl hydrogen replacement (condensation) products, viz. stilbenes and β -alkylstyrenes. Methyl acrylate reacts to give conjugated addition (hydrocondensation) products, methyl esters of β -aryl and β -alkyl propionic acids.

Introduction

Arylation of vinyl compounds by aryl iodides and aryl bromides has been carried out in the presence of a palladium catalyst (usually palladium acetate), a tertiary phosphine and a base [1]. The reaction with aliphatic halides does not proceed under these conditions [2]. More recently, nickel complexes RNiBrL_2 were shown to react stoichiometrically with vinyl compounds to give vinyl hydrogen replacement products [3]. As zinc powder is capable of recovering nickel catalysts in the homocoupling reaction of aryl bromides [4], we suggested that the system nickel complex/zinc powder could be used to catalyse the condensation of organic bromides with vinyl compounds.

Results and discussion

We found that nickel complexes catalyse the condensation of styrenes with aryl [5] and alkyl [6] bromides in the presence of zinc and pyridine in acetonitrile.



The reaction mechanism is probably similar to the generally accepted mechanism of the vinyl hydrogen replacement reaction in the presence of palladium complexes

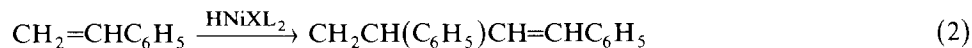
Table 1

Condensation of bromobenzene with styrene in the presence of different amounts of the catalyst, styrene, zinc and pyridine (bromobenzene, 1 mmol; CH₃CN, 3 ml; 65 °C, 4 h)

| No. | Styrene (mmol) | Zinc (mmol) | Pyridine (mmol) | Catalyst (mol.%) | Stilbene yield ^a (%) | DPB yield ^b (%) |
|-----|----------------|-------------|-----------------|------------------|---------------------------------|----------------------------|
| 1 | 4 | 1 | 4 | 5 | 92 | 25 |
| 2 | 4 | 1 | 4 | 10 | 100 | 25 |
| 3 | 4 | 1 | 4 | 2 | 64 | 19 |
| 4 | 4 | 1 | 4 | 5 ^c | 75 | 26 |
| 5 | 2 | 1 | 4 | 5 | 75 | 11 |
| 6 | 1 | 1 | 4 | 5 | 36 | 5 |
| 7 | 4 | 5 | 4 | 5 | 100 | 37 |
| 8 | 4 | 2 | 4 | 5 | 100 | 31 |
| 9 | 4 | 0.5 | 4 | 5 | 80 | 23 |
| 10 | 4 | 0.25 | 4 | 5 | 38 | 12 |
| 11 | 4 | 1 | 8 | 5 | 90 | 9 |
| 12 | 4 | 1 | 0 | 5 | 50 | 55 |

^a GLC, based on bromobenzene. ^b GLC, based on styrene. ^c Catalyst: NiCl₂·6H₂O (0.05 mmol) and Ph₃P (0.1 mmol).

[7] and includes the steps (a) reduction of NiCl₂ to Ni⁰ by zinc; (b) oxidative addition of RBr to Ni⁰; (c) incorporation of PhCH=CH₂ at the C-Ni bond in RNiBrL₂, the product of reaction b; and (d) β-elimination of the hydride nickel complex HNiBrL₂ from the intermediate RCH₂CH(Ph)NiBrL₂. Unlike HPdBrL₂, the hydride nickel complex is probably more stable and catalyses the side reaction of styrene dimerization [8] to produce 1,3-diphenylbut-1-ene (DPB).



The dependence of the yields of the major products on the reagent ratio was studied for the reaction of bromobenzene with styrene (Table 1).

Reaction 1 takes place readily in the presence of the complex (Ph₃P)₂NiCl₂ introduced in an amount of 0.05 to 0.1 molar equivalent with respect to RBr (nos. 1 and 2 in Table 1). This catalyst can be replaced by a 1/2 mixture of NiCl₂·6H₂O and Ph₃P (No. 4). Excess styrene (Nos. 1, 5 and 6) and zinc (Nos. 1, 7 and 8) favour complete conversions, whereas decreasing the quantity of zinc to less than 0.5 molar equivalent causes a rapid decrease in the yield of stilbene (No. 10). It appears that zinc is required to recover Ni⁰ from HNiBrL₂ in each catalytic cycle. This suggestion is substantiated by the isolation of Py₂ZnBr₂ in stoichiometric quantities from reaction mixtures after the completion of the process [6c]. The addition of pyridine increases the yield of stilbene and decreases that of DPB (Nos. 11 and 12); that is, pyridine promotes reaction 1 and inhibits reaction 2. Strong organic bases such as Et₃N completely suppress reaction 1. The reaction practically does not go at ambient temperature. At 85 °C, the reaction mixture undergoes rapid blackening because of the formation of nickel metal.

Examples of the use of organic bromides in reaction 1 are given in Table 2. The reaction is an effective route to monosubstituted stilbenes via the condensation of substituted phenyl bromides with styrene (Nos. 14–21) in Table 2 or bromobenzene with substituted styrenes (Nos. 22 and 23). Substituents such as fluorine, chlorine,

Table 2
 Condensation of organic bromides with styrene (RBr/styrene/zinc/pyridine/catalyst = 1/2-4/1/4/0.05, CH₃CN, 65°C, 4 h)

| No. | RBr | Styrene | Product | Yield (%) ^a | m.p. (°C) or b.p. (°C/mmHg) | Refs. |
|-----|---|--|--|------------------------|--------------------------------|-------|
| 13 | C ₆ H ₅ Br | CH=CHC ₆ H ₅ | C ₆ H ₅ CH=CHC ₆ H ₅ | 86 (100) | 124 | 11 |
| 14 | 4-MeC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 4-MeC ₆ H ₄ CH=CHC ₆ H ₅ | 77 (83) | 119 | 12 |
| 15 | 3-MeC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 3-MeC ₆ H ₄ CH=CHC ₆ H ₅ | (100) | | |
| 16 | 2-MeC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 2-MeC ₆ H ₄ CH=CHC ₆ H ₅ | (32) | | |
| 17 | 4-ClC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 4-ClC ₆ H ₄ CH=CHC ₆ H ₅ (I) | 75 (87) | 128 | 11 |
| 18 | 4-FC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 4-FC ₆ H ₄ CH=CHC ₆ H ₅ | 70 (88) | 124 | 11 |
| 19 | 4-MeOC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 4-MeOC ₆ H ₄ CH=CHC ₆ H ₅ (II) | 67 (75) | 136 | 11 |
| 20 | 4-MeCOC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 4-MeCOC ₆ H ₄ CH=CHC ₆ H ₅ | 60 (71) | 141 | 13 |
| 21 | 4-MeOCOC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₅ | 4-MeOCOC ₆ H ₄ CH=CHC ₆ H ₅ | 51 (87) | 157 | 13 |
| 22 | C ₆ H ₅ Br | CH ₂ =CHC ₆ H ₄ Cl-4 | I | (65) | | |
| 23 | C ₆ H ₅ Br | CH ₂ =CHC ₆ H ₄ OMe-4 | II | (64) | | |
| 24 | 4-MeCOC ₆ H ₄ Br | CH ₂ =CHC ₆ H ₄ OMe-4 | 4-MeCOC ₆ H ₄ CH=CHC ₆ H ₄ OMe-4 | 48 | 174 | 14 |
| 25 | cyclo-C ₆ H ₁₃ Br | CH ₂ =CHC ₆ H ₅ | C ₆ H ₅ CH=CH-cyclo-C ₆ H ₁₃ | 65 (100) | 108-110/4 | 15 |
| 26 | 3-C ₅ H ₁₃ Br | CH ₂ =CHC ₆ H ₅ | C ₆ H ₅ CH=CHCH(C ₂ H ₅)C ₃ H ₇ | 45 (75) | 94-96/4 | 6c |
| 27 | 2-C ₅ H ₁₁ Br | CH ₂ =CHC ₆ H ₅ | C ₆ H ₅ CH=CHCH(CH ₃)C ₃ H ₇ | 58 (81) | 72-76/4 | 6c |
| 28 | 2-C ₃ H ₇ Br | CH ₂ =CHC ₆ H ₅ | C ₆ H ₅ CH=CH(CH ₃)CH ₃ | 23 (50) | 52-55/4 | 16 |
| 29 | 1-C ₆ H ₁₃ Br | CH ₂ =CHC ₆ H ₅ | C ₆ H ₅ CH=CHC ₆ H ₁₃ | 11 (36) | 91-94/4 | 17 |
| 30 | 1-C ₄ H ₉ Br | CH ₂ =CHC ₆ H ₅ | C ₆ H ₅ CH=CHC ₄ H ₉ | 15 (31) | 66-71/4 | 18 |

^a Yields based on RBr (values in parentheses are GLC yields).

hydrocarbon groups or groups containing oxygen do not interfere with the reaction, whereas groups containing nitrogen block the process. Aryl bromides are far more active than aryl chlorides. Chlorobenzene reacts with styrene to give DPB as the major product and stilbene in only a negligible amount (below 5%). The possibility of the preparation of disubstituted stilbenes is demonstrated by the reaction of 4-bromoacetophenone with 4-methoxystyrene (No. 24). Secondary alkyl bromides give much higher yields of β -alkylstyrenes (Nos. 26–28) compared with primary ones (Nos. 29 and 30). It appears that with secondary alkyl bromides, the conformation of the intermediate $\text{RCH}_2\text{CH}(\text{Ph})\text{NiBr}_2$ capable of β -elimination is formed less easily.

Reaction 1 is regio- and stereo-selective, for it only gives the products of styrene β -hydrogen replacement having the *E* configuration. All the stilbenes formed in this reaction are crystalline solids with m.p.s of *E* isomers. The ^1H NMR spectra of the stilbenes and β -alkylstyrenes obtained are characterized by $J(\text{H}_\alpha\text{H}_\beta)$ spin-spin coupling constants of ca. 16 Hz, which is indicative of their *trans*-configuration. The most characteristic bands in the IR spectra substantiate disubstituted ethylene-type product structures with a *trans*-arrangement of the hydrogen atoms ($962\text{--}967\text{ cm}^{-1}$).

With methylacrylate instead of styrene, the same reaction gives conjugated addition (hydrocondensation) products [9].



Unlike styrene, methyl acrylate does not give the dimer. Biphenyl, however, appears in the absence of pyridine (Nos. 32–34, Table 3). Decreasing the amount of methyl acrylate results in a decrease in the yield of methyl-3-phenyl propionate (No. 32). The introduction of excess methyl acrylate or pyridine increases the yield substantially (Nos. 34 and 35). The reaction run with methyl acrylate, pyridine and acetonitrile freshly distilled over CaH_2 gave only 14% yield of methyl-3-phenylpropionate (No. 36), whereas the addition of water (1.5 molar equivalents) to reagents dried in this way increased the yield to 48% (No. 37). Thus “the worse, the better” (the drier the reagents, the poorer the yield). The addition of a large excess of D_2O to a dried or non-dried reaction mixture causes the formation of β -deuterated

Table 3

Condensation of bromobenzene with methyl acrylate in the presence of different amounts of bromobenzene, methyl acrylate, pyridine and water (zinc, 1 mmol; catalyst, 0.05 mmol; CH_2CN , 3 ml; 65°C ; 4 h)

| No. | Bromobenzene (mmol) | Methyl acrylate (mmol) | Pyridine (mmol) | Water (mmol) | Methyl-3-phenyl propionate yield ^a (%) | Biphenyl yield ^a (%) |
|-----|---------------------|------------------------|-----------------|--------------|---|---------------------------------|
| 31 | 1 | 4 | 4 | <i>b</i> | 74 | 0 |
| 32 | 1 | 1 | 0 | <i>b</i> | 9 | 13 |
| 33 | 1.5 | 1 | 0 | <i>b</i> | 10 | 65 |
| 34 | 1 | 4 | 0 | <i>b</i> | 47 | 7 |
| 35 | 1 | 1 | 4 | <i>b</i> | 50 | 0 |
| 36 | 1 | 4 | 4 | <i>c</i> | 14 | 0 |
| 37 | 1 | 4 | 4 | 1.5 <i>c</i> | 48 | 0 |

^a GLC, based on bromobenzene. ^b Non-dried reagents. ^c Dried reagents.

Table 4

Hydrocondensation of organic bromides with methyl acrylate (RBr/methyl acrylate/zinc/pyridine/catalyst = 1/4/1/4/0.05, CH₃CN, 65 °C, 4 h, non-dried reagents)

| No. | RBr | Product | Yield (%) | m.p. (°C) or b.p. (°C/mmHg) | Refs. |
|-----|---|---|----------------------|-----------------------------|-------|
| 38 | C ₆ H ₅ Br ^a | C ₆ H ₅ CH ₂ CH ₂ COOMe | 57 (74) ^b | 68–70/2 | 19 |
| 39 | 4-ClC ₆ H ₄ Br | 4-ClC ₆ H ₄ CH ₂ CH ₂ COOMe | 30 (45) | 85–86/2 | 20 |
| 40 | 4-MeOC ₆ H ₄ Br | 4-MeOC ₆ H ₄ CH ₂ CH ₂ COOMe | 62 (82) | 35–36 | 21 |
| 41 | 4-MeOCOC ₆ H ₄ Br | 4-MeOCOC ₆ H ₄ CH ₂ CH ₂ COOMe | 55 (72) | 29–30 | 22 |
| 42 | cyclo-C ₆ H ₁₃ Br | cyclo-C ₆ H ₁₃ CH ₂ CH ₂ COOMe | 36 (55) | 82–83/4 | 23 |
| 43 | 2-C ₅ H ₁₁ Br | C ₃ H ₇ CH(CH ₃)CH ₂ CH ₂ COOMe | 41 (60) | 65–66/10 | 24 |

^a The addition of D₂O (10 mol. equivalents) results in the formation of C₆H₅CH₂CHDCOOMe. ^b The yields are based on RBr (values in parentheses are GLC yields).

methyl-3-phenyl propionate as the only product, whereas the use of CD₃CN or C₅D₅N does not result in deuteration. The ¹H NMR spectrum of non-deuterated methyl-3-phenyl propionate contains two distorted triplets corresponding to α- and β-protons (with respect to the carbomethoxy group). In the spectrum of the deuterated compound, the lower field triplet of the β-protons is transformed into a doublet, the doublet to triplet intensity ratio being 2/1. The observations show that the presence of water is necessary for successfully carrying out reaction 3.

Examples of the use of various aryl and alkyl bromides in reaction 3 are given in Table 4.

Reaction 3 probably follows the mechanism of reaction 1, including the step of the formation of the intermediate RCH₂CH(Z)NiBrL₂. With styrene (Z = Ph), β-elimination of hydrogen follows, whereas with methyl acrylate (Z = COOMe), the intermediate compound undergoes protonation at the C–Ni bond to give a saturated product. In the latter case, it is not impossible that stability towards β-elimination depends on the formation of a coordination bond between nickel and the oxygen of the carbomethoxy group which hinders the elimination proceeding with the participation of a vacancy in the nickel coordination sphere.

A further study is needed to determine the forms in which nickel occurs after the reaction event and the mechanism of their recovery to produce the catalytically active form.

Recently, a similar catalytic system was used to study the condensation of bromobenzene and styrene and methyl acrylate in THF [10]. Unlike the reaction studied in this work, that reported by Boldrini et al. [10] was claimed to give both saturated and unsaturated products from methyl acrylate. Also, the participation of water in the formation of the saturated product was rejected.

Experimental

Aryl and alkyl bromides were used without further purification. Pyridine and acetonitrile were dried over KOH and CaCl₂, respectively, and distilled over CaH₂ in an argon flow. The complex (Ph₃P)₂NiCl₂ was prepared following a known procedure [25]. 4-Chloro- and 4-methoxy-styrenes were made by coupling 4-chloro- and 4-methoxyphenyl-magnesium bromides with vinyl bromide [26]. All reactions were performed in an argon atmosphere. GLC analyses were done on a Tsvet-110

chromatograph (column 2000×3 mm, 3% SE-30 on Chromaton-*N*-super, gas carrier helium, naphthalene as internal reference). ^1H NMR spectra were recorded on a Tesla instrument (100 MHz). All the products isolated have been described earlier (see the refs. in Tables 2 and 4).

4-Methoxystilbene. A mixture of 4-bromoanisole (0.5 ml, 4 mmol), styrene (1.84 ml, 16 mmol), pyridine (1.28 ml, 16 mmol) and zinc powder (0.26 g, 4 mmol) in 12 ml of acetonitrile was blown through by argon for 10 min. The complex $(\text{Ph}_3\text{P})_2\text{NiCl}_2$ (0.13 g, 0.2 mmol) was then added and the mixture was stirred for 4 h at 65°C . The products were transferred to a separating funnel, decomposed with 4% HCl, and extracted with ether. The ether layer was dried over CaCl_2 , the solvent was distilled off, and the residue was recrystallized from methanol to obtain 4-methoxystilbene (0.5 g, 67%), m.p. 135°C [11].

1-Phenyl-3-methylhex-1-ene. 1-Phenyl-3-methylhex-1-ene (1.53 g, 58%, b.p. $72\text{--}76^\circ\text{C}/4$ mmHg [6c]) was prepared from 2-bromopentane (1.9 ml, 15 mmol) as described above. This product was isolated by distillation.

Methyl-4-methylheptanoate. Argon blown for 10 min through a mixture of acetonitrile (20 ml), methyl acrylate prepared by shaking with water in a separating funnel (3.62 ml, 40 mmol), 2-bromopentane (1.26 ml, 10 mmol), pyridine (3.2 ml, 40 mmol) and zinc powder (0.65 g, 10 mmol). The complex $(\text{Ph}_3\text{P})_2\text{NiCl}_2$ was then added, and the mixture was stirred for 4 h at 65°C . The products were decomposed with 4% HCl and extracted with ether in a separating funnel; the ether extracts were dried over CaCl_2 ; ether was distilled off; and the residue was subjected to distillation to obtain methyl-4-methyl heptanoate (0.65 g, 41%), b.p. $65\text{--}66^\circ\text{C}/10$ mmHg [24].

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