Nickel-Catalysed Hydroalkoxylation Reaction of 1,3-Butadiene: Ligand Controlled Selectivity for the Efficient and Atom-Economical Synthesis of Alkylbutenyl Ethers

Sandra Bigot, Mohammed Samir Ibn El Alami, Alexis Mifleur, Yves Castanet, Isabelle Suisse,* André Mortreux, and Mathieu Sauthier^{*[a]}

Alkyl ethers are commonly obtained by the Williamson reaction between an alcohol and a haloalkane in the presence of a base. In addition to often rather limited selectivity, limitations arise from the formation of stoichiometric amounts of salts and both more efficient and atom-economical processes are thus needed. The telomerisation reaction allows the clean and efficient synthesis of octa-2,7-dienyl ethers from 1,3-butadiene and an alcohol as nucleophile (Scheme 1).^[1] The use of palladium salts with phosphines,^[2] and more recently, carbene ligands^[3] affords highly active and robust catalysts thus allowing scale-up of the telomerisation reaction to industrial quantities for the selective synthe-



Scheme 1. Nickel-catalysed transformations of 1,3-butadiene in the presence of an alcohol: Telomerisation, hydroalkoxylation and dimerisation reactions.

sis of 1-octene from 1,3-butadiene. In addition, this transformation has proven to be an efficient synthetic tool to graft C8 alkadienyl chains onto glycerol, higher polyols, sugars or starch for the synthesis of amphiphiles.^[4] On the other hand, the direct mono-addition of an alcohol to a diene leading to shorter alkenyl ethers is much less studied. This transformation, also referred to as degenerative telomerisation or hydroalkoxylation, yields linear (cis and trans) **4** and branched **5** butenyl ethers (OC4; Scheme 1). However, this reaction is rarely selective because the by-products that arise from telomerisation (linear **2** and branched **3** alkyl octadienyl ethers (OC8)) and butadiene dimerisation^[5] (1,3,7-octatriene **6** and isomers) are also usually formed.^[6]

Dewhirst first described the selective synthesis of butenyl ethers **4** and **5** from butadiene and ethanol in the presence of high loadings of rhodium trichloride as a catalyst.^[7] With π -allyl palladium chloride complexes and phenol as the solvent, Smutny reported the formation of phenoxybutenes in low yield (30%) along with *ortho-* and *para*-butenylphenols and oligomerisation/dimerisation products.^[8] Palladium-based catalysts also allowed access to butenyl ethers with high selectivities in dilute methanolic solutions.^[9]

Reports of nickel-catalyzed telomerisation and hydroalkoxylation reactions are rare. The use of a Ni(acac)₂/NaBH₄/ phenyldiisopropoxyphosphine (acac=acetylacetonate) mixture had the propensity to produce a mixture of methoxybutenes and methoxyoctadienes, along with some 1,3,7-octatrienes.^[10] Attempts to obtain similar results with triphenylphosphine, triphenylphosphite or triisopropoxyphosphine were unsuccessful. Later work with different catalytic combinations of nickel sources, monophosphines and either phenolic^[11] or alcoholic nucleophiles gave similar results but again without particular selectivity.^[12–13] Selective and accessible catalysts are necessary in order to generate butenyl ethers and herein we report our recent progress in this field.

Our studies on the ethoxylation of butadiene were carried out with different nickel precursors combined with simple phosphines. In a typical experiment, the nickel precursor bis(cyclooctadiene)nickel(0) or a mixture of bis(acetylacetonate)nickel(II)/sodium borohydride (1:1.5) and the ligand were stirred for 5 min in ethanol in a Schlenk tube. Then, liquid butadiene was added at -15 °C and the mixture was heated to the desired temperature for 17 h. After cooling



[[]a] Dr. S. Bigot, Dr. M. S. I. El Alami, A. Mifleur, Prof. Y. Castanet, Dr. I. Suisse, Prof. A. Mortreux, Prof. M. Sauthier UCCS (Unité de Catalyse et de Chimie du Solide) Université Lille Nord de France - ENSCL BP 90108, 59652 Villeneuve d'Ascq (France) Fax: (+33)3-20-33-63-01 E-mail: isabelle.suisse@ensc-lille.fr mathieu.sauthier@univ-lille1.fr

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Table 1. Hydroalkoxylation/telomerisation of butadiene with ethanol in the presence of nickel catalysts. $^{[a]}$

Entry	Nickel source	Ligand	Butadiene	5	4	OC8	C8
			Conv. [%]	[%]	[%]	[%]	[%]
1 ^[b]	Ni(acac) ₂ /NaBH ₄	PPh ₃	36	0	0	0	99
2	Ni(acac) ₂ /NaBH ₄	dppe	0	0	0	0	0
3	Ni(acac) ₂ /NaBH ₄	dppp	0	0	0	0	0
4	Ni(acac) ₂ /NaBH ₄	dppb	94	76	24	<2	$<\!2$
5	$Ni(cod)_2$	dppb	93	72	23	<2	5
6	Ni(acac) ₂	dppb	0	0	0	0	0
7	Ni(acac) ₂ /NaBH ₄	dpppen	52	26	23	9	42
8	Ni(acac) ₂ /NaBH ₄	xantphos	0	0	0	0	0
9	Ni(acac) ₂ /NaBH ₄	binap	0	0	0	0	0
10	Ni(acac) ₂ /NaBH ₄	L1	86	50	8	19	23
11	Ni(acac) ₂ /NaBH ₄	L2	100	65	22	8	5

[a] Conditions: butadiene = 11.1 mmol, Ni/NaBH₄/ligand/butadiene = 1:1:1.5:80, EtOH = 10 mL, T = 80 °C, t = 17 h. acac = acetylacetonate, cod = 1,5-cyclooctadiene, dppe = 1,2-bis(diphenylphosphino)ethane, dppb = 1,4-bis(diphenylphosphino)butane, dpppen = 1,5-bis(diphenylphosphino)pentane, binap = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, dppp = 1,3-bis(diphenylphosphino)propane. [b] 2 equivalents PPh₃ with respect to Ni.

and venting, the solution was analyzed by GC and the products were quantified with heptane as the internal standard. Branched versus linear products could be differentiated. In the presence of Ni(acac)₂/NaBH₄ and PPh₃, as documented previously, the reaction yields dimerization products with a high selectivity (Table 1, entry 1).^[5] On the other hand, the use of the diphosphines dppe (1,2-bis(diphenylphosphino)ethane) and dppp (1,3-bis(diphenylphosphino)propane) did not result in any butadiene conversion. Very surprisingly, the use of the dppb (1,4-Bis(diphenylphosphino)butane) ligand gave drastically different results (Table 1, entry 4), vielding butenyl ethers 4 and 5 in higher than 95% selectivity with a 94% conversion of butadiene after 17 h at 80°C. The branched product 5 was obtained as the major butenyl ether isomer (5/4=3). No reaction was observed if Ni(acac)₂ is used without sodium borohydride but very similar results were obtained with $[Ni(cod)_2]$ (cod = 1,5-cyclooctadiene; Table 1, entries 4 and 5). A nickel(0) species thus appears to be a key catalytic intermediate. The use of Ni(acac)₂/NaBH₄ proved to be very practical as compared with the use of airsensitive [Ni(cod)₂]. This catalyst combination was thus retained for the rest of the study. A rather limited conversion of 1,3-butadiene is observed with the 1,5-diphenylphosphinopentane (dpppen; Table 1, entry 7) ligand, yielding a quite large amount of dimerization products. In contrast to the result obtained with the dppb ligand, the 5/4 ratio is close to 1, thus showing that this regioselectivity can be tuned according to the catalyst structure. These results also suggest that the size of the bidentate ligand framework plays a crucial role in the selectivity of the reaction. Xantphos shows no catalytic activity, possibly because of coordination of the oxygen atom of the ligand to the metal, thus leading to highly coordinated complexes that exhibit low reactivity. We then turned our attention towards diphosphines that would give rise to a seven-atom heterocycle upon coordination to a metal center.



Application of binap (2,2'-bis(diphenylphosphino)-1,1'-binaphthyl) proved completely fruitless. Bis(aminophosphines) L1 and L2 were then synthesized in a single step from diamines by phosphinylation with two equivalents of chlorodiphenylphosphine in the presence of triethylamine.^[14] L1 and L2 have an electron-donor character due to the presence of two nitrogen atoms close to the phosphorous atoms, which should have an effect on the selectivity, as found by comparison of phosphine, phosphite and phosphonite ligands used for the nickel(0)-catalyzed addition of phenol to butadiene.^[11] Interestingly, both ligands show a reasonable propensity to produce butenyl ethers (Table 1, entries 10 and 11). These results reinforce the importance of the ligand backbone in inducing high hydroalkoxylation selectivity. The effect of the dppb ligand on the observed selectivities is particularly relevant. It seems clear that the flexibility of the ligand backbone is a key factor in allowing the reaction to proceed selectively towards C4 ethers. The dppb ligand has previously resulted in unusual outcomes in several catalytic reactions such as in the chemoselective palladium-catalyzed methoxycarbonylation of 1,3-butadiene.^[15] Unprecedented reactivity^[16] and linear regioselectivity have also been observed in platinum-catalyzed hydroformylation of alkenes by well-defined ligand bridged dinuclear platinum hydride species.^[17] Oligomeric (dppb)palladium–acyl complexes have also been identified during studies of CO insertion into palladium alkyl bonds.^[18] Accordingly, we suspect that such oligomeric (dppb)nickel allylic species could be responsible for this particular reactivity/selectivity.

With dppb as a standard ligand, some reaction parameters were then tuned in order to delineate the best reaction conditions (Table 2). The amount of sodium borohydride was

Table 2. Optimisation of the hydroalkoxylation/telomerisation of butadiene with ethanol in the presence of the Ni(acac)₂/dppb/NaBH₄ catalytic system.^[a]

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Entry	L/Ni	NaBH₄∕ Ni	Butadiene Conv. [%]	5 [%]	4 [%]	OC8 [%]	C8 [%]
1	1.5	0.5	94	75	25	<2	<2
2	1.5	4	58	70	30	< 2	<2
3	0.5	1	65	50	50	<2	<2
4	1	1	91	46	44	5	5
5	2.5	1	29	79	21	<2	<2
6 ^[b]	1.5	1	52	41	35	15	9
7 ^[c]	1.5	1	56	74	21	3	<2

[a] Conditions: butadiene = 11.1 mmol, Ni/butadiene = 1:80, EtOH = 10 mL, T = 80 °C, t = 17 h. [b] 1,3-butadiene = 56 mmol, Ni/butadiene = 1:400, EtOH = 10 mL, the reaction was performed in a steel high-pressure reactor. [c] 1,3-butadiene = 56 mmol, Ni/butadiene = 1:400, EtOH = 20 mL, the reaction was performed in a steel high-pressure reactor.

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varied with respect to the nickel loading. The amount of sodium borohydride needed is clearly catalytic and the best results were obtained with a NaBH₄/Ni ratio ranging from 0.5 to 1. A higher ratio led to drastically reduced conversions that can be attributed to nickel boride formation. Nevertheless, high selectivities for butenyl ethers were maintained. The best ligand/nickel ratio was found to be around 1.5 equivalents and larger amounts did not improve selectivity and were shown to be detrimental to 1,3-butadiene conversion. Finally, the amount of 1,3-butadiene was increased to 400 equivalents with respect to nickel (Table 2, entries 6 and 7) which required twice as much ethanol to limit the formation of dimers and to obtain almost unchanged selectivities compared to the previous tests with 80 equivalents of 1,3-butadiene.

We further studied the reaction with other alcohols (Table 3). Methanol failed to react if the catalyst was prepared in this solvent. Methanol appears to react with

Table 3. Hydroalkoxylation reaction of various alcohols with the Ni-(acac)_2/dppb/NaBH₄ catalytic system.^[a]

Entry	Alcohol/co-solvent	Butadiene Conv. [%]	4+5 [%]	OC8 [%]	C8 [%]
1	MeOH	0	0	0	0
2	MeOH/THF ^[b]	89	98	<2	<2
3	PhCH ₂ OH	95	98	<2	<2
4	iPrOH	0	0	0	0
5	iPrOH/EtOH ^[c]	15	75	25	<2
6 ^[b]	tBuOH	0	0	0	0
7 ^[c]	PhOH/THF ^[b]	0	0	0	0

[a] Conditions: butadiene = 11.1 mmol, Ni/butadiene = 1:80, alcohol = 10 mL, T = 80 °C, t = 17 h. [b] The nickel precursor was formed in 2 mL THF at room temperature for 10 min, and ethanol (10 mL) or phenol (5 g) were added. [c] The reaction was run with *i*PrOH (5 mL) and EtOH (5 mL), only ethoxylation products were obtained.

sodium borohydride before the nickel(II) precursor is reduced as evidenced by the rapid dihydrogen evolution that was observed in the early seconds of reaction. The catalyst was therefore generated beforehand by the reaction of NaBH₄ and Ni(acac)₂ in THF. This alternative procedure allowed the ready synthesis of methyl butenyl ethers with high selectivities and yields that are comparable to those obtained with ethanol. From our results, primary alcohols react readily in the hydroalkoxylation reaction and benzyl alcohol also afforded a mixture of butenyl ethers in good yields. In contrast, more highly substituted alcohols failed to react and no reaction products (butenyl ethers, dimerization or telomerisation products) were formed with isopropanol and tertbutanol and prior preparation of the catalyst in an aprotic solvent did not result in any improvement. A reaction involving a 1:1 mixture of ethanol and isopropanol was run to gain more insight into the nature of the reaction. Only the products of ethoxylation (4 and 5) were observed, in low vield, along with the OC8 telomerisation products, showing that isopropanol is not only unreactive but is also detrimental to the catalyst activity and selectivity. Lastly, aromatic alcohols, as exemplified by phenol, failed to yield the desired products.

Hydroalkoxylation of butadiene occurs with high selectivity for the formation of butenyl ethers. The nickel precursor and ligand used are readily available and are easily reacted with sodium borohydride to generate the catalyst. A strong ligand dependency has been observed and the use of the dppb ligand is critical to access highly selective catalysts under relatively mild reaction conditions. Further work to gain a better understanding of the specific role of the ligand in the unprecedented selectivity revealed, as well as further improvements, are underway.

Experimental Section

In a typical catalytic experiment, the nickel precursor Ni(acac)₂ (35 mg, 0.14 mmol), the diphosphine (0.21 mmol) and sodium borohydride (NaBH₄; 5.3 mg; 0.14 mmol), were introduced into a Schlenk tube closed with a rotaflo stop cock. Distilled and degassed ethanol (10 mL), previously cooled to 0°C, was then added. The tube was further cooled down to -20°C. A precise volume of butadiene (11.1 mmol, 0.6 g, 1 mL) was condensed in a Schlenk tube cooled with an acetone/dry ice mixture and transferred into the reaction mixture. Finally the reactor was heated at 80°C and stirred with a magnetic stirrer for 17 h. After the reaction, the system was cooled and excess gaseous butadiene was vented before chromatographic analysis.

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