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Catalytic allylation of phenols : chloride-free route towards epoxy resins

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Selective O-allylation of bisphenol A: the ultimate goal

Abstract

The O-allylation of bisphenol A is attempted with the most selective catalysts for O-allylation of phenols reported in the previous chapters. Both ruthenium as well as palladium catalysts are capable of selectively performing single and double O-allylation. The choice of the solvent is of key importance and the use of an excess of diallyl ether results in relatively high yields for the bisallyl ether of bisphenol A, while maintaining high selectivity for O-allylation.

9.1 Introduction

Multiple allylations of BPA have been reported in literature, but these studies do not make use of allyl alcohol (or diallyl ether), but either allyl halides,¹⁻⁵ allyl acetates,^{6,7} or allyl carbonates⁸ are employed as the allylating agent. A stoichiometric amount of base is also often employed to create phenolate anions *in situ*, increasing the nucleophilicity on the O-position.

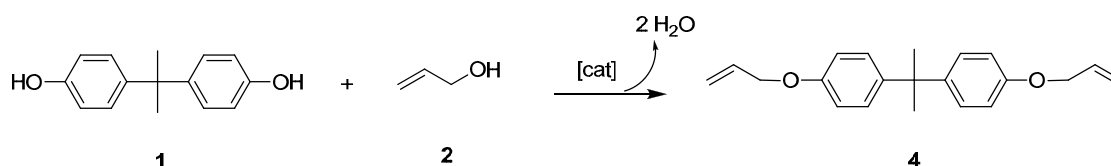
In the previous chapters, the detailed study of mono-O-allylation of phenols was reported. 4-*Tert*-butylphenol was mainly used as a model substrate for bisphenol A (BPA), in order to simplify the analysis of the multiple products that can be formed. The investigation has led to a better understanding of the mechanism for O-allylation of phenols with allyl alcohol and revealed the requirements for a suitable catalyst and optimal reaction conditions. Several very selective catalytic systems were found for O-allylation of phenols, like [RuCp(dppb)](OTs) (Chapter 2) and [RuCp(PPh₃)₂](OTs) (Chapter 4) in the presence of acid, the immobilized [RuCp(PPh₃)(resinPhPPh₂)](OTs) in the presence of acid (Chapter 6) and Pd(OAc)₂ with dppdmp as the ligand (Chapter 8). Having several options in hand for the selective O-allylation of a monophenol with allyl alcohol into an allyl phenyl ether, BPA was used as the ultimate substrate.

The goal is to perform a double O-allylation as was proposed in the introduction of this thesis (Scheme 9.1). The main problem arising from using BPA as a substrate is that a large number of different products can be formed (Scheme 9.2). Whereas in the allylation of 4-*tert*-butylphenol a total of four products are observed, in the allylation of BPA a total of fourteen different products can theoretically be obtained, increasing the importance of the use of highly selective catalysts.

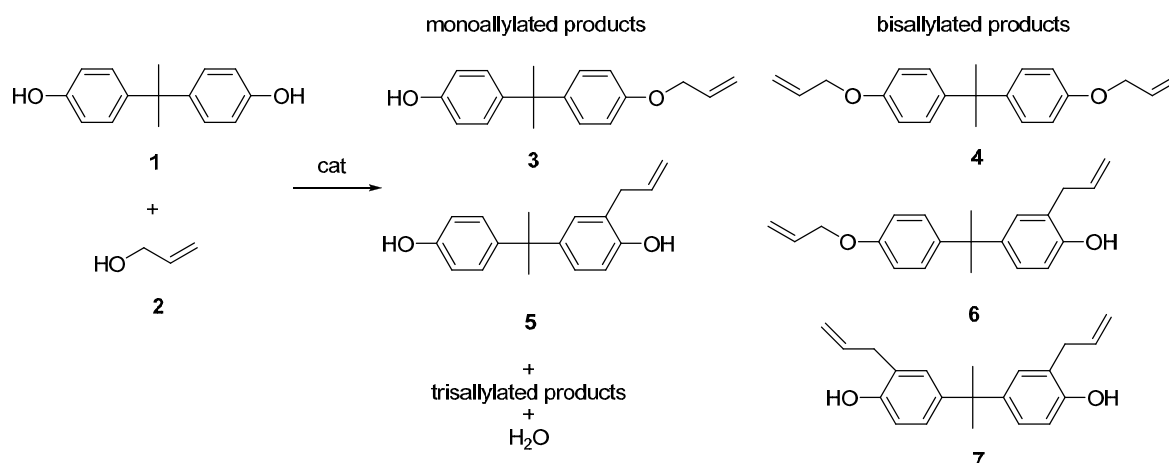
9.2 Results and discussion

9.2.1 Product analysis

Apart from the increase of possible products when 4-*tert*-butylphenol was replaced with BPA, also the analytical method used to quantify the product formation has to be changed.



Scheme 9.1. Proposed chlorine-free and salt-free process towards synthesis of bisglycidyl bisphenyl A ether.



Scheme 9.2. Structures of mono- and bisallylated products **3-7** formed in allylation of BPA with allyl alcohol. Structures of trisallylated products are not shown.

Detection with GC was not possible and HPLC was used to quantify the product formation. Products **3-7** are efficiently separated by means of HPLC and characterized with LC/MS. The O-allylated product **3** and **4** were also synthesized by reported procedures,⁴ characterized by NMR spectroscopy and LC/MS. Response factors in UV-detection proved to be independent of the allylic substitution. The phenol moieties are initially monoallylated, either O- or C-allylation, before one of the rings is substituted with a second allyl moiety, which only occurs after longer reaction times. This product development is observed for all the allylation reaction with BPA. The trisallylated products are only present in very low concentrations for the less selective reactions. These products could not be separated efficiently. The selectivity for O-allylation is defined by calculating the percentage of O-allylated products (**3** + **4**; Scheme 9.2) on the total amounts of products formed.

9.2.2 Catalytic allylation of BPA

The selection of the most selective catalyst found during this research project and their reactivity in the O-allylation of BPA with allyl alcohol is shown in Table 9.1. The ratio BPA over catalyst used was 500/1 and therefore conversions of **1** (Scheme 9.2) after one hour are higher compared to the reactions with 4-*tert*-butylphenol reported previously, where a substrate over catalyst ratio of 1000/1 was generally used. However, when the number of OH-moieties is considered, conversions of 4-*tert*-butylphenol and BPA are similar. [RuCp(PPh₃)₂](OTs) in the presence of acid (*p*-toluenesulfonic acid = HOTs) shows to be reasonably selective for O-allylation of BPA with a conversion of 46% of BPA and a selectivity of 80% for O-allylation (entry 1). However, when compared to the selectivity for O-allylation of 4-*tert*-butylphenol (>90%), this selectivity is considerably lower. The lower selectivity towards O-allylation is most likely caused by the fact that product **4** is formed after

Table 9.1. Allylation of BPA using several catalytic systems and conditions ^a

entry	catalytic system	allylating agent	temperature (°C)	conversion of 1 (%) and selectivity for O-allylation (%) ^b		yield of 4 after 3 h (%)
				1 h	3 h	
1	[RuCp(PPh ₃) ₂](OTs)	allyl alcohol	60	46 (80)	46 (63)	14
2	[RuCp(PPh ₃) ₂](OTs)	diallyl ether	60	91 (68)	98 (48)	30
3	[RuCp(PPh ₃) ₂](OTs)	allyl acetate	60	81 (74)	90 (52)	18
4 ^c	[RuCp(PPh ₃) ₂](OTs)	allyl alcohol	60	22 (70)	31 (50)	5
5	[RuCp(dppb)](OTs)	allyl alcohol	80	62 (66)	89 (65)	20
6 ^d	[RuCp(PPh ₃)(resinPhPPh ₂)](OTs)	allyl alcohol	80	80 (80)	81 (76)	25
7 ^e	Pd(OAc) ₂ + dppdmp	allyl alcohol	100	38 (100)	54 (100)	10

^a Reaction conditions: ratio BPA/allyl alcohol/[Ru]/AgOTs/HOTs = 500/2000/1/2/20, toluene.

^b Selectivity towards O-allylation indicated in parentheses. O-allylation = **3** + **4**; C-allylation = **5-7** + trisallylated compounds.

^c *n*-heptane was used as solvent

^d Reaction conditions: ratio BPA/allyl alcohol/[Ru]/AgOTs/HOTs = 50/200/1/2/2, toluene.

^e Reaction conditions: ratio BPA/allyl alcohol/Pd(OAc)₂/dppdmp = 500/2000/1/4, 100 °C.

two equilibrium reactions and therefore less likely to form compared to a mono-O-allylated phenol.

When allyl alcohol is replaced with diallyl ether as the allylating agent, conversions are higher (entry 2). C-allylation commences at an earlier stage during the reaction, due to the higher initial conversion, since diallyl ether formation from allyl alcohol is not occurring. If allyl acetate is used as the allylating agent (entry 3), the reaction is only active in the presence of *p*-toluenesulfonic acid, most likely to form acetic acid and thus preventing formation of the relatively strong coordination acetate anion. With the use of allyl acetate, allylating agent of choice in patents of Dow Chemicals,^{6,7} selectivity for O-allylation is not increased. For reactions reported in these patents [RuCpCl(PPh₃)₂] is used as the catalyst, but selectivity is not reported in a clear manner and a very high catalyst concentration is used (2 mol%). When such an experiment is reproduced (for exact procedure see experimental part), selectivity for O-allylation is low (41%) and a large amount of trisallylated product is obtained (52%). The use of allyl acetate does not lead to more selective reactions and allyl alcohol or diallyl ether remain the choice for more attractive allylating agents. The use of *n*-heptane as a solvent gives significantly lower conversions and selectivity (entry 4) compared to toluene. This can be explained by the low solubility of BPA in *n*-heptane at the reaction temperature. The desired products (**3** + **4**) however, are soluble and therefore the reaction of these products into the undesired C-allylated products is faster than the O-allylation of **1**. The use of [RuCp(dppb)](OTs) as the catalyst (entry 5), gave low selectivity, but this catalyst was somewhat more selective compared to the [RuCp(PPh₃)₂](OTs) after 3 hours reaction time with high conversion. The use of the immobilized Ru-catalyst (entry 6) gave a highly

selective reaction towards O-allylation and the catalyst was effectively recovered (leaching was 1.0 % of total Ru-content on support). Finally, $\text{Pd}(\text{OAc})_2$ in combination with the dppdmp ligand gave excellent selectivity towards O-allylation (entry 7), but after three hours, mainly product **3** was formed and only 10% of the bisallyl ether **4** is obtained.

The equilibrium reaction of O-allylation is controlled by the amount of water that dissolves in the organic phase. Toluene is beneficial to obtain a reasonable conversion; it is quite apolar so that water solubility in the reaction medium is low, but it is not too apolar for BPA to dissolve at reaction temperature. An extra benefit from using toluene is that the desired product is completely soluble at room temperature, while the starting material BPA is not and conveniently crystallizes from the reaction mixture in high purity.

9.2.3 Allylating agents as solvent

The reaction with $[\text{RuCp}(\text{PPh}_3)_2](\text{OTs})$ as the catalyst in the presence of acid and with diallyl ether as the allylating agent gave the highest yield of **4** (30% after 3 hours). Selectivity for O-allylation is however not very high and a large amount of C-allylated products are formed. In an attempt to improve the selectivity of the reaction, different solvent systems were investigated and the results are shown in Table 9.2.

When the reaction is performed in allyl alcohol as the solvent, no conversion of **1** is observed (entry 1) and only formation of diallyl ether is detected. With diallyl ether as the solvent (entry 2), the reaction proceeds very selective towards O-allylation, but mainly product **3** is

Table 9.2. Allylation of BPA in the presence of Ru- or Pd-based catalysts with different solvent systems ^a

entry	catalyst	solvent	conversion of 1 (%) and selectivity for O-allylation (%) ^b		yield of 4 after 3 h (%)
			1 h	3 h	
1	$[\text{RuCp}(\text{PPh}_3)_2]^+$	allyl alcohol	0 (-)	0 (-)	0
2	$[\text{RuCp}(\text{PPh}_3)_2]^+$	diallyl ether (DAE)	47 (100)	54 (94)	9
3	$[\text{RuCp}(\text{PPh}_3)_2]^+$	DAE / toluene = 2/1	86 (85)	95 (82)	50
4	$[\text{RuCp}(\text{PPh}_3)_2]^+$	DAE / toluene = 1/1	95 (81)	95 (72)	51
5	$[\text{RuCp}(\text{PPh}_3)_2]^+$	DAE / toluene = 1/2	96 (68)	96 (64)	46
6	$[\text{RuCp}(\text{PPh}_3)_2]^+$	DAE / heptane = 2/1	55 (91)	80 (86)	23
7	$[\text{RuCp}(\text{PPh}_3)_2]^+$	DAE / heptane = 3/1	80 (92)	98 (84)	49
8	$[\text{RuCp}(\text{PPh}_3)_2]^+$	DAE / heptane = 4/1	78 (93)	90 (88)	38
9 ^c	$\text{Pd}(\text{OAc})_2$ + dppdmp	DAE / toluene = 2/1	12 (100)	28 (100)	2 (24)

^a Reaction conditions: ratio BPA/allyl alcohol/ $[\text{RuCpCl}(\text{PPh}_3)_2]/\text{AgOTs}/\text{HOTs}$ = 500/2000/1/2/20, 60 °C, total solvent volume = 2.5 ml

^b Selectivity towards O-allylation indicated in brackets. O-allylation = **3** + **4**; C-allylation = **5-7** + trisallylated compounds.

^c Reaction conditions: ratio BPA/allyl alcohol/ $\text{Pd}(\text{OAc})_2/\text{dppdmp}$ = 500/2000/1/4, 100 °C, total solvent volume = 2.5 ml. Yield of **4** in parentheses determined after 20 hours reaction time. Selectivity for O-allylation remains 100%.

formed and only 9% of **4** is formed after 3 hours reaction time. When the solvent is made more apolar by using a mixture of diallyl ether and toluene (entry 3), conversion of **1** and yield of **4** is increased in a major way and 50% of **4** (based on **1**) is formed, a very high yield for a product formed via two equilibrium reactions. Making the solvent more apolar by increasing the amount of toluene on diallyl ether causes selectivity to decrease (entry 4 and 5). Apart from toluene as the apolar component in the reaction mixture, also *n*-heptane can be used. When the results from entries 6-8 are compared to that of entry 3, slightly less *n*-heptane than toluene should be used for an optimal selectivity for O-allylation. This is obviously caused by the higher apolarity of *n*-heptane than that of toluene. Finally, besides the $[\text{RuCp}(\text{PPh}_3)_2]^+$ catalyst, the Pd-catalytic system proved to be highly selective for O-allylation. When a diallyl ether / toluene mixture is used as the solvent, the reaction is completely selective for O-allylation, however, conversion of **1** after 3 hours is considerably lower than that of the Ru-based catalytic system. After 20 hours, only O-allylated products are detected while the yield for **4** increases to 24% based on **1**. Even longer reaction times did not result in higher conversion, indicating complete deactivation of the catalyst.

9.2.4 Industrial application

When the allylation reaction described above with BPA as the substrate is implemented in an industrial process, several things should be noted. Due to the thermodynamical preference of C-allylation over O-allylation of phenols, the reaction will eventually build up C-allylated side products, of which the concentration depends on a combination of catalyst structure and reaction time and is independent on allylating agent. It is therefore of key importance that the reaction is halted before C-allylated products form when performed in a batch reaction. In a continuous process, both water, forming a separate phase in the reaction mixture, and the desired product needs to be efficiently removed from the reaction mixture while feeding it with new starting materials. The very low polarity of product **4** compared to **1** and water could be used to separate these compounds by extraction. Diallyl ether should be used as (co-) solvent, which can be efficiently synthesized from allyl alcohol. With the use of $[\text{RuCp}(\text{PPh}_3)_2](\text{OTs}) + \text{HOTs}$ as the catalytic system, extremely high turnover number can be achieved based on allyl alcohol (> 200,000), as was already demonstrated in Chapter 4.

9.3 Conclusions

[RuCp(PPh₃)₂](OTs) in the presence of acid is very selective for *O*-allylation of BPA and high yields (~50%) of the bisallyl ether of BPA are obtained. Allyl alcohol or diallyl ether perform equally well or better compared to allyl acetate as allylating agent. The choice of solvent is crucial for both high conversion as well as high selectivity for *O*-allylation. Diallyl ether seems to be the allylating agent of choice for reaction with BPA and is best used as solvent in the presence of an apolar co-solvent, like toluene or *n*-heptane. Pd(OAc)₂ with the phosphine ligand dppdmp as catalyst is even more selective compared to the Ru-based system. C-allylated products are not detected, even after longer reaction times. Catalyst stability is however the bottleneck when using this catalyst, as was already discussed in Chapter 8.

The atom-efficiency of this catalytic reaction, is much higher compared to the conventional saline reaction, where a phenolate salt is reacted with an allyl halide. However, for industrial application, the catalytic reaction, being a double equilibrium reaction with a maximum yield of 50%, is at this stage of development much more difficult to perform compared to the conventional saline reaction, giving nearly quantitative yields.

9.4 Experimental

General remarks. All reactions were performed under an argon atmosphere using standard Schlenk techniques. Solvents were dried and distilled by standard procedures and stored under argon. Bisphenol A was obtained as a gift from Hexion Speciality Chemicals and used as received. Procedures for catalyst syntheses have been reported in the previous chapters.

General procedure for catalytic reactions with Ru-catalysts. 1.25 mmol of BPA, 2.5 μmol of Ru-complex, 5.0 μmol of AgOTs and 0.05 mmol HOTs were charged into the reaction vessel and flushed with argon. Degassed and dried toluene or *n*-heptane (2.5 ml, unless stated otherwise) was added and the mixture was stirred for 5 minutes. The allyl donor was added and the reaction mixture was heated to reaction temperature. Samples were taken at certain time intervals and analyzed by HPLC.

Procedure for catalytic reactions with Pd-catalyst. 1.25 mmol of BPA, 2.5 μmol of Pd(OAc)₂ and 10 μmol of dppdmp were charged into the reaction vessel and flushed with argon. Degassed and dried toluene (2.5 ml; unless stated otherwise) was added and the mixture was stirred for 5 minutes. The allyl donor was added and the reaction mixture was heated to reaction temperature. Samples were taken at certain time intervals and analyzed by HPLC.

Procedure of Dow patent reaction. A mixture of 285 mg (1.25 mmol) BPA, 36 mg [RuCpCl(PPh₃)₂] (2 mol%) and 2.5 g (25 mmol) allyl acetate under an argon atmosphere is stirred at 95 °C. After 6 hours, the mixture was analyzed by HPLC.

HPLC analysis. HPLC analysis was performed with a Summit Dual Gradient HPLC system (Dionex) connected with a PDA3000 diode array detector (Dionex). The HPLC was equipped with an Alltima HP C18 3u reverse phase column (150x4.6 mm), with a flow of 1 ml/min and injection volume of 10 µl of a solution of the reaction mixture in acetonitrile. The gradient conditions were at t = 0-17 (minutes) acetonitrile (%) / water (%) = 50/50, t = 17-23 acetonitrile 100%, t = 23-30 acetonitrile (%) / water (%) = 50 / 50. Spectroscopic data for **3-7** corresponded with that reported in literature.¹

9.5 References

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