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Selective O-allylation of bisphenol A: toward a chloride-free route for epoxy resins

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The O-allylation of bisphenol A (BPA) has been performed with the most selective catalysts for O-allylation of phenols reported previously. Both the cyclopentadienyl–ruthenium catalysts and the palladium–diphosphine catalysts are capable of selectively performing single and double O-allylation of BPA. An intriguing solvent effect is observed; the choice of the solvent is of key importance for both conversion and selectivity. The use of an excess of diallyl ether as allylating agent results in relatively high yields of the bisallyl ether of bisphenol A, while maintaining the high selectivity for O-allylation.

Keywords: allylation; bisphenol A; allyl alcohol; diallyl ether; catalysis

Introduction

In the context of the development of an environmentally benign catalytic route to epoxy resins, a two-step route is proposed consisting of the O-allylation of bisphenol A, followed by the oxidation of the two olefinic groups to obtain the bisglycidyl ether of BPA (Scheme 1).[1] Several studies of the allylation of BPA have been reported, but these studies do not make use of allyl alcohol (or its condensed derivative diallyl ether); instead allyl halides,[2–8] allyl acetate[1,9] or allyl carbonate[10–13] are employed as the allylating agent. A stoichiometric amount of base is often necessary to create the phenolate anions *in situ*, thus increasing the nucleophilicity of the O-position. Allyl alcohol, however, would be a much more attractive allyl donor, since only water is co-produced in allylation reactions. Thus allyl alcohol can be considered as a 'green' reagent, but only if no other reagents are necessary in stoichiometric amounts to control activity and selectivity.

In our previous work detailed studies of O-allylation of phenols have been reported.[14–18] 4-*Tert*-butylphenol was mainly used as a model substrate for bisphenol A, in order to simplify the analysis of the multiple products that can be formed. Our investigation has led to a better understanding of the mechanism for O-allylation of phenols with allyl alcohol and revealed the specific requirements for a good catalyst and optimal reaction conditions. The conversion of the phenol into the allyl phenyl ether turned out to be limited due to the presence of an equilibrium reaction. Not only allyl alcohol but also diallyl ether, the condensation product of two molecules of allyl alcohol, turned out to be a suitable allylating agent. Having established the requirements for the selective O-allylation of a phenol with allyl alcohol to form an allyl phenyl ether, BPA has now been used as the ultimate substrate.

The goal of the research thus was to perform a double O-allylation as shown in Scheme 1, without the need for stoichiometric additives. Whereas in the allylation of 4-*tert*-butylphenol a total of four products was observed, in the allylation of BPA a total of 14 different products can theoretically be obtained, underlining the importance of the development of highly selective catalysts. Several catalytic systems that were found to yield the best results for the selective O-allylation of phenols have now been used in the catalytic allylation of BPA and the results are described below. The structures of the catalysts [RuCp(dppb)](OTs),[14] [RuCp(PPh_3)$_2$](OTs),[16] the immobilized complex [RuCp(PPh_3)(resinPhPPh_2)](OTs)[18] and Pd(OAc)$_2$ with the diphosphine ligand dppdmp[17] are shown in Fig. 1.

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 was used as received. Procedures for the synthesis of the catalysts have been reported previously by us.[14,16–18]

Catalytic Procedures

Reactions with Ru catalysts

A 1.25 mmol aliquot of BPA, 2.5 μmol of Ru complex, 5.0 μmol of AgOTs and 0.05 mmol HOTs (*p*-toluenesulfonic acid) 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 min. 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.

Reactions with Pd catalyst

A 1.25 mmol aliquot of BPA, 2.5 μmol of Pd(OAc)$_2$ and 10 μmol of dppdmp were charged into the reaction vessel and flushed

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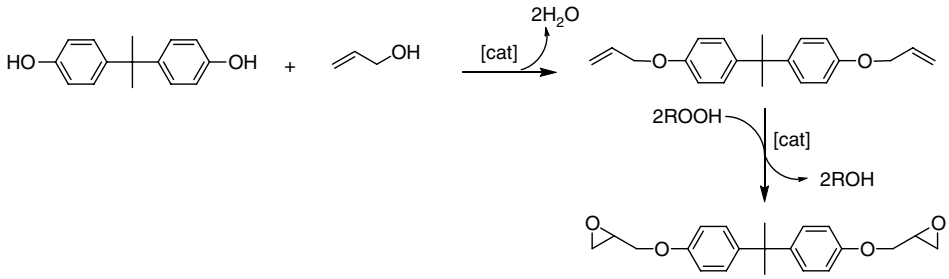


Scheme 1. Proposed chlorine-free and salt-free process towards bisglycidyl ether of bisphenol A.

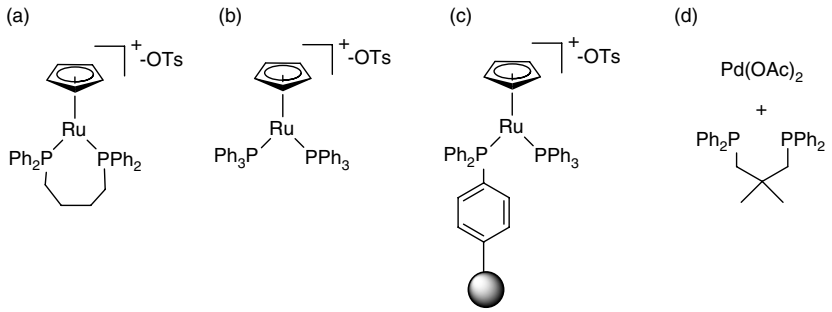


Figure 1. Structure of the catalyst used in the allylation of bisphenol A: (a) [RuCp(dppb)](OTs); (b) [RuCp(PPh_3)$_2$](OTs); (c) [RuCp(PPh_3) (resinPhPPh_2](OTs); (d) Pd(OAc)$_2$ + dppdmp.

with argon. Degassed and dried toluene (2.5 ml unless stated otherwise) was added and the mixture was stirred for 5 min. 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(PPh_3)$_2$] (2 mol%) and 2.5 g (25 mmol) allyl acetate under an argon atmosphere is stirred at 95 °C. After 6 h the reaction 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 C_{18} 3u reverse phase column (150 × 4.6 mm), with a flow rate of 1 ml min^{-1} and an injection volume of 10 µl of a solution of the reaction mixture in acetonitrile. The gradient conditions were at t = 0–17 min acetonitrile (%) : water (%) = 50 : 50, t = 17–23 min acetonitrile 100%, t = 23–30 min acetonitrile (%) : water (%) = 50 : 50. Spectroscopic data for compounds **3–7** corresponded with those reported in literature.[2]

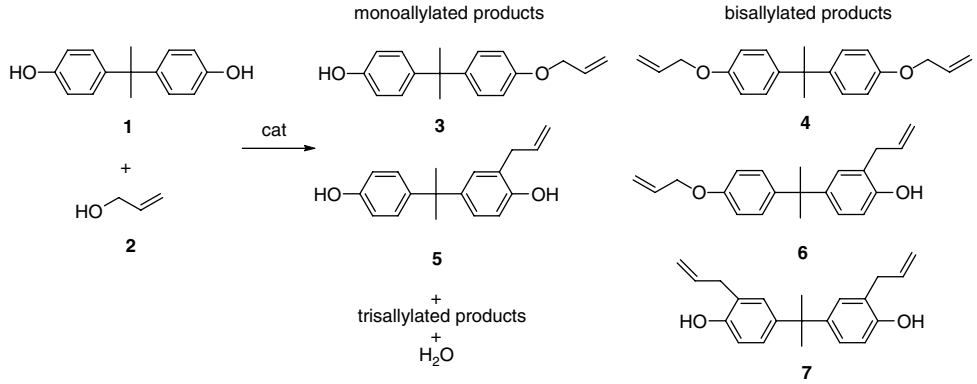
Results and Discussion

Product Analysis

The main problem arising from the use of BPA as the substrate is that a large number of different products can be formed (Scheme 2). In the allylation of 4-*tert*-butylphenol a total of four products are observed, that are conveniently separated with GC. In the allylation of BPA a total of 14 different products can theoretically be obtained, each with high molecular weight precluding the use of GC as an analytical tool. It was found that products **3**–**7** are efficiently separated by means of HPLC and characterized with LC/MS. The O-allylated products **3** and **4** were also synthesized by reported procedures,[5] characterized by NMR spectroscopy and LC/MS. The response factors in UV detection proved to be independent of the allylic substitution. The BPA is initially mono-allylated, yielding either the O- (**3**) or C-allylated (**5**) product, before one of the rings is substituted with a second allyl moiety, which only occurs after longer reaction times. This product development is observed in all the allylation reactions of BPA. The tris-allylated 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 discussed below is defined by calculating the percentage of O-allylated products (**3** + **4**; Scheme 2) on the total amounts of products formed.

Catalytic Allylation of BPA

The results of the use of the most selective catalysts in the O-allylation of BPA with allyl alcohol are given in Table 1. The ratio BPA over catalyst used was 500 : 1 and therefore conversions of **1** (Scheme 2) after 1 h are higher compared with 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(PPh_3)$_2$](OTs) in the presence of acid (*p*-toluenesulfonic acid = HOTs) is reasonably selective for O-allylation of BPA with a conversion of 46% of BPA and a selectivity of 80% for O-allylation after 1 h (entry 1). This selectivity is considerably lower than the selectivity for O-allylation of 4-*tert*-butylphenol (>90%), which is most likely caused by the fact that product **4** is only formed after two equilibrium reactions. When allyl alcohol is replaced with diallyl ether as the allylating



Scheme 2. Structures of mono- and bisallylated products **3**–**7** formed in allylation of BPA with allyl alcohol. Structures of possible trisallylated products are not shown.

Table 1. Allylation of BPA using several catalytic systems and conditions[a]

Entry	Catalytic system	Allylating agent	Temperature (°C)	Conversion of **1** (%) (selectivity for O-allylation, %)[b] 1 h	3 h	Yield of **4** after 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.

agent, the conversion of BPA is 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.

In the patents of Dow Chemicals,[1,9] allyl acetate is claimed to be superior to allyl alcohol as an allylating agent. If allyl acetate is used as the allylating agent in our reaction conditions (entry 3), the catalyst is only active in the presence of *p*-toluenesulfonic acid, most likely to form acetic acid and thus prevent the formation of the relatively strongly coordinating acetate anion. Although the use of allyl acetate with our catalytic system results in higher activity, the overall selectivity for O-allylation decreases. In the reactions described in the Dow patents,[1,9] $[RuCpCl(PPh_3)_2]$ is used as the catalyst, but a very high catalyst concentration is used (2 mol%) and the selectivity is not reported in a clear manner. Most likely the phenol content was determined by means of titration of the phenol residues, which makes it impossible to determine the amount of C-allylation. When such a patent experiment is reproduced (see Experimental section), the analysis results of our HPLC method show that the selectivity for O-allylation is rather low (41%) and a large amount of trisallylated product is obtained (52%). The use of allyl acetate thus results in lower selectivity for O-allylation and we therefore conclude that allyl alcohol or diallyl ether remain the more attractive allylating agents.

The use of *n*-heptane as solvent results in significantly lower conversion and selectivity (entry 4) compared with 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 relatively rapid. The use of [RuCp(dppb)](OTs) as the catalyst (entry 5) gives relatively low selectivity, but after 3 h reaction time this catalyst is slightly more selective than $[RuCp(PPh_3)_2](OTs)$ with high conversion. The use of the immobilized Ru-catalyst (entry 6) gives a highly selective reaction towards O-allylation and the catalyst was effectively recovered (leaching 1% of total Ru-content on support). Finally, $Pd(OAc)_2$ in combination with the ligand dppdmp gives excellent selectivity towards O-allylation (entry 7), but after 3 h mainly the monosubstituted product **3** is 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 and thus the water solubility is low, but it is not too apolar for BPA to dissolve at reaction temperature. A further benefit of the use of toluene is that the desired product is completely soluble at room temperature; as the starting material BPA is not soluble it conveniently crystallizes from the reaction mixture in high purity, thus allowing recovery of the starting material from the reaction products.

Table 2. Allylation of BPA in the presence of Ru- or Pd-based catalysts with different solvent systems[a]

Entry	Catalyst	Solvent	Conversion of **1**(%) (selectivity for O-allylation, %)[b] 1 h	3 h	Yield of **4** after 3 h (%)
1	$[RuCp(PPh_3)_2]^+$	Allyl alcohol	0 (—)	0 (—)	0
2	$[RuCp(PPh_3)_2]^+$	Diallyl ether (DAE)	47 (100)	54 (94)	9
3	$[RuCp(PPh_3)_2]^+$	DAE : toluene = 2 : 1	86 (85)	95 (82)	50
4	$[RuCp(PPh_3)_2]^+$	DAE : toluene = 1 : 1	95 (81)	95 (72)	51
5	$[RuCp(PPh_3)_2]^+$	DAE : toluene = 1 : 2	96 (68)	96 (64)	46
6	$[RuCp(PPh_3)_2]^+$	DAE : heptane = 2 : 1	55 (91)	80 (86)	23
7	$[RuCp(PPh_3)_2]^+$	DAE : heptane = 3 : 1	80 (92)	98 (84)	49
8	$[RuCp(PPh_3)_2]^+$	DAE : heptane = 4 : 1	78 (93)	90 (88)	38
9[c]	$Pd(OAc)_2$ + dppdmp	DAE : toluene = 2 : 1	12 (100)	28 (100)	2 (24)

[a] Reaction conditions: ratio BPA : allyl alcohol : $[RuCpCl(PPh_3)_2]$: AgOTs : 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 : $Pd(OAc)_2$: dppdmp = 500 : 2000 : 1 : 4, 100 °C, total solvent volume = 2.5 ml. Yield of **4** in parentheses determined after 20 h reaction time. Selectivity for O-allylation remains 100%.

Allylating Agents as Solvent

The reaction with $[RuCp(PPh_3)_2](OTs)$ 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 h). The selectivity for O-allylation is, however, not very high and a large amount of C-allylated products is formed. In an attempt to improve the selectivity of the reaction, different solvent systems were investigated and the results are shown in Table 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 selectively, but mainly product **3** is formed and only 9% of **4** is formed after 3 h reaction time. When the reaction medium 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 that is formed via two equilibrium reactions. Making the solvent more apolar by increasing the amount of toluene on diallyl ether causes a decrease in selectivity (entries 4 and 5). Also *n*-heptane was used as the apolar component in the reaction mixture. When the results from entries 6–8 are compared with that of entry 3, it appears that slightly less *n*-heptane than toluene should be used for an optimal selectivity for O-allylation, which obviously can be related to the lower polarity of *n*-heptane. Finally, besides the $[RuCp(PPh_3)_2]^+$ catalyst, the Pd-containing 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 BPA after 3 h is considerably lower than in the Ru-based catalytic system. After 20 h, only O-allylated products are detected while the yield for **4** increases to 24% based on **1**. Longer reaction times did not result in higher conversion, indicating complete deactivation of the catalyst. This deactivation also prevents possible C-allylation, as C-allylation mostly occurs to an appreciable extent later in the reaction, when a high concentration of O-allylated product is reached.

Industrial Application

When the described allylation reaction with BPA as the substrate is implemented in an industrial process, several things should be considered. Owing to the thermodynamic preference of C-allylation over O-allylation of phenols, the reaction eventually will build up C-allylated side products, of which the concentration depends on a combination of catalyst structure and reaction time and is independent on the 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 with **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 $[RuCp(PPh_3)_2](OTs)$ + HOTs as the catalytic system, extremely high turnover numbers can be achieved based on allyl alcohol (>200 000), as has already been demonstrated.[16]

A schematic representation of a possible continuous process is shown in Fig. 2. In an ideal case, diallyl ether should be synthesized from pure allyl alcohol, catalyzed by the Ru-catalyst, forming only water as co-product (reactor 1: **R1** in Figure 2). The resulting mixture is then separated in a separation system (**S2**); a suitable method would be distillation. The isolated diallyl ether is used as allylating agent (in excess) in the O-allylation of BPA (reactor 2, **R2**), catalyzed by the same catalyst present in reactor 1. An inert solvent (like *n*-heptane) could be added during, but also after, the reaction to create an apolar system from which the phenolic products and catalyst would precipitate, occurring in **S2**. This separation is believed to be the bottleneck of such a process, since many compounds are present in the mixture from **R2** and in particular products **3** and **4** proved to be difficult to separate. A bleed of C-allylated products would be necessary, in order to prevent accumulation of these compounds. However, the catalyst should be recycled and therefore a heterogeneous catalyst would be favored.[18] If the catalyst was homogeneous, it would also be removed from the process, which is only commercially acceptable when the bleed is very small or the catalyst is highly active with high turnover numbers. Compounds containing two phenol moieties hardly dissolve in heptanes and are therefore less difficult to retrieve from the reaction mixture. However, the selective separation of C-allylated product from **3** is expected to be

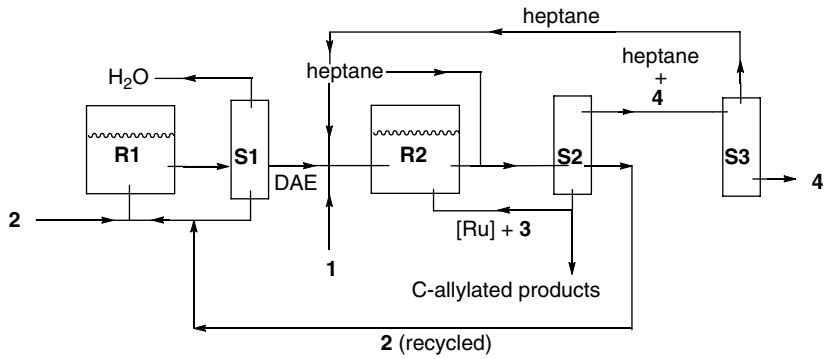


Figure 2. Schematic overview of a possible process for the catalytic allylation of bisphenol A. DAE = diallyl ether. R = reactor; S = separation system.

very difficult. Finally, heptanes are removed from the the bisallyl ether of BPA by means of distillation in separation system 3 (**S3**).

Conclusions

$[RuCp(PPh_3)_2](OTs)$ in the presence of a strong acid is very selective for the O-allylation of BPA and relatively high yields (~50%) of the bisallyl ether of BPA have been obtained. Allyl alcohol or diallyl ether can be used equally well or even better than allyl acetate as allylating agent. The choice of solvent is crucial for both high conversion and 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, such as toluene or *n*-heptane. $Pd(OAc)_2$ with the phosphine ligand dppdmp as catalyst is even more selective compared with the Ru-based system; C-allylated products are not detected, even after longer reaction times. For this catalyst system, however, catalyst stability is the limiting factor, as has been observed earlier.[17] For the reactions of BPA a careful analysis with HPLC of all possible products is very important, since simple titrations of phenol content will not detect C-allylated products.

The potential atom-efficiency of this catalytic reaction is much higher than that of the conventional process using epichlorohydrin. However, for industrial application the developed catalytic reaction, being a double equilibrium reaction for which we have reached a maximum yield of the desired product of 50%, is at this stage much more difficult to perform than the conventional salt-forming reaction that results in nearly quantitative yields. Also the challenging epoxidation reaction[19] that needs to be performed to obtain the final epoxy resin component makes further research necessary.

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