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Title: On the origin of primary aromatic amines in food packaging materials

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Abstract: Primary aromatic amines (PAAs) are substances that can be transferred from food packaging materials into foodstuffs and are "possibly carcinogenic to humans." The formation of PAAs from multilayer packaging materials consisting of aromatic polyurethane (PU) adhesives, occurs from the reaction between residual isocyanic monomers that have migrated to the surface of the inner layer of the package and water molecules making contact with the same plastic surface. However, for foods subjected to thermal treatments, an alternative formation of PAAs should also be taken into consideration. Due to the detrimental effect of the temperature, some secondary bonds (namely allophanate and biuret bonds) displaced on the main PU backbone may be disrupted, originating neo-formed isocyanic monomers. The migration of these monomers from the adhesive layer across the inner sealing film can lead to PAAs as soon as they come into contact with the water molecules of the liquid or high aw packaged food. Although the existence and the mechanisms of the formation of allophanate and biuret linkages during the polymerization process with poly-isocyanates has been known for a long time, the negative impact on public health possibly arising from the migration of the neo-formed isocyanic monomers into the foods during thermal treatments seems to have not been fully perceived, with special regard to preservative heat treatments such as pasteurization and sterilization. In this viewpoint article, after covering both chemical and physical aspects involved in the formation of PAAs, especially in thermally-treated PU-based multilayer packaging materials, we have stressed the necessity for a more careful consideration of the risks associated with the potential formation of PAAs, in a first instance by strict compliance with the provisions included in the current European legislation. The necessity for alternative analytical tools for the PAAs quantification is also highlighted.

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On the origin of primary aromatic amines in food packaging materials

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Abstract

Primary aromatic amines (PAAs) are substances that can be transferred from food packaging materials into foodstuffs and are “possibly carcinogenic to humans.” The formation of PAAs from multilayer packaging materials consisting of aromatic polyurethane (PU) adhesives, occurs from the reaction between residual isocyanic monomers that have migrated to the surface of the inner layer of the package and water molecules making contact with the same plastic surface. However, for foods subjected to thermal treatments, an alternative formation of PAAs should also be taken into consideration. Due to the detrimental effect of the temperature, some secondary bonds (namely allophanate and biuret bonds) displaced on the main PU backbone may be disrupted, originating neo-formed isocyanic monomers. The migration of these monomers from the adhesive layer across the inner sealing film can lead to PAAs as soon as they come into contact with the water molecules of the liquid or high a_w packaged food. Although the existence and the mechanisms of the formation of allophanate and biuret linkages during the polymerization process with poly-isocyanates has been known for a long time, the negative impact on public health possibly arising from the migration of the neo-formed isocyanic monomers into the foods during thermal treatments seems to have not been fully perceived, with special regard to preservative heat treatments such as pasteurization and sterilization. In this viewpoint article, after covering both chemical and physical aspects involved in the formation of PAAs, especially in thermally-treated PU-based multilayer packaging materials, we have stressed the necessity for a more careful consideration of the risks associated with the potential formation of PAAs, in a first instance by strict compliance with the provisions included in the current European legislation. The necessity for alternative analytical tools for the PAAs quantification is also highlighted.

Keywords: food packaging; neo-formation; primary aromatic amine (PAA); polyurethane (PU) adhesive; thermal treatment

Introduction

Multilayer packages consist of several layers of different materials (generally from two layers up to 15 layers) on top of one another to yield an aggregate thickness defined, by convention, to be less than 250 μm (thicker structures are typically identified as “sheet” materials) (Dunn, 2009). The combination of different plastic materials, sometimes including metal or cellulosic substrates, underlies the rapid popularity of laminated structures, as they allow for fine-tuning the final performance of the ultimate package to precisely match the food’s requirement for an extended shelf life.

Several converting operations concern multilayered packaging materials, namely printing, coating, laminating, and finishing. Lamination, in particular, is the operation that allows for the holding together of different layers for the entire life cycle of the package. Although extrusion lamination and coextrusion are widely adopted processes, the lamination mediated by an adhesive (often called “tie” layer) finds application in most converting lines due to the ease of manufacturing and the low cost involved (Rosato, 1998) (Figure 1a). Among the wide assortment of adhesive systems commercially available, polyurethane (PU) adhesives are well-known for superior flexibility, mechanical and adhesion properties, and weathering resistance (Malucelli *et al.*, 2005), which play an important role when severe processing/environmental conditions (e.g., high temperature of retort processing, aggressive chemicals, or high-moisture environments) may affect the package performance and the quality of the food inside it.

PU adhesives come from reactive systems usually including two main components, one carrying isocyanic moieties (NCO-terminated) and the other containing hydroxyl groups (OH-terminated). These components, when mixed together, undergo chemical reactions (i.e., chain extension) that bind the applied materials into a solid layer of high molecular weight PU adhesive (Figure 2, scheme 1). The adhesive components react after lamination, further increasing the molecular weight of the PU adhesive to achieve the required performance (Meier-Westhues, 2007). Because the adhesives are made of reactive chemicals that are expected to polymerize by linear

extension and/or cross-link, government food-safety-related agencies (e.g., the Food and Drug Administration [FDA] in the United States and the European Food Safety Authority [EFSA]) have established a strict legislative body to control the risk associated with the potential migration of toxic substances from the adhesives to the food (e.g., unreacted residuals), which in turn might also have harmful effects on the consumers' health (de Fátima Poças & Hogg, 2007). In the case of multilayer packaging materials (e.g., pouches, trays, bags, wrappers, etc.), in particular, one of the main issues related to PU adhesive systems is the potential presence of primary aromatic amines (PAAs) in the food matrix (Ellendt, Gutsche, & Steiner, 2003). The potential risk associated with PAAs arises from the suspected carcinogenic activity of some of them that can affect humans (e.g., 2,4 and 2,6-diaminotoluene and 4,4-methylenedianiline), as stated by the International Agency for Research on Cancer (Vineis & Pirastu, 1997).

Unlike the U.S. regulation, which has banned the aromatic-based PU adhesives to the advantage of fully aliphatic systems (U.S. Food and Drugs Administration, 2000), the European legislation establishes that "...plastic materials and articles shall not release primary aromatic amines in a detectable quantity into food or food simulant. The detection limit is 0.01 mg of substance per kg of food or food stimulant (namely, 10 ng g⁻¹ of food). The detection limit applies to the sum of primary aromatic amines released (expressed as aniline)" (European Commission, 2011). Excluded from this provision are the species reported in Table 1 of Annex I of the same regulation (e.g., 1,3-phenylenediamine and 1,3-benzenedimethanamine).

The most popular method for the quantification of PAAs is the spectrophotometric method, developed by the German Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) (Brauer & Funke, 1991). This method is based on the derivatization with N-(1-naphthyl)ethylene-1,2-diamine dihydrochloride (NEDA) of the amines present in the aqueous food simulant (acetic acid 3%, w/v) after the migration test. The final colored compound is then measured spectrophotometrically at 550 nm (i.e., the maximum absorbance of the aniline derivative). Quantification of PAAs is expressed as equivalent to aniline. The main drawback associated with this

method is its non-selectivity, which may lead to an overestimation of the total amount of PAAs found in the aqueous simulant (Aznar, Canellas, & Nerín, 2009). To overcome this issue, several methods have been developed during the last decade (Akyüz & Ata, 2008; Andrisano, Gotti, DiPietra, & Cavrini, 1994; Aznar *et al.*, 2009; Noguerol-Cal, López-Vilariño, Fernández-Martínez, Barral-Losada, & González-Rodríguez, 2008; Shelke, Sanghi, Asthana, Lamba, & Sharma, 2005). Most modern analytical techniques based on mass spectrometry and advances in ionization processes for non-volatile compounds have made use of UHPLC–MS and their hyphenated techniques such as UHPLC–MS/TQ and, most recently, UHPLC–Q-TOF/MS (Mattarozzi, Lambertini, Suman, & Careri, 2013; Pezo, Fedeli, Bosetti, & Nerín, 2012). All of these methods, besides targeting increasing sensitivity, demonstrate that the unequivocal identification of all compounds present in food packaging materials, including the non-intentionally added substances (NIAS), can be achieved.

The origin of PAAs is primarily linked to residual (unreacted) isocyanic monomers that migrate across the sealing layer, which is generally highly amorphous low-density polyethylene (LDPE) or cast polypropylene (C-PP) (Brede, Skjevraak, & Herikstad, 2003) from the PU adhesive to the surface of the laminate. Within this specific time span, i.e. immediately following the lamination process and before the packaging operations, the possibly migrated isocyanic monomer can uniquely come in contact with the air (thus, in contact with the surrounding environmental moisture) between two adjacent coils of the laminated material wound in a reel. The reaction between the residual isocyanic monomer and water molecules leads to the formation of primary amines (Figure 2, scheme 2a). In practice, this issue is commonly addressed by storing the reels of the laminate materials for the time necessary to consume the free isocyanic monomer by: i) further reaction with the main adhesive system, or ii) reacting, after migration, with the water molecules of the environmental humidity always present in traces between the coils of the laminate (European Commission, 2006; Flexible Packaging Europe, 2008). In the latter case, the isocyanic monomers will first react with the water molecules to form primary amines (Figure 2, scheme 2a), which in turn will react with newly-migrated isocyanic molecules to generate (poly)urea (Figure 2, scheme 2b), a whitish, solid, and non-

toxic compound that, due to a high melting point, may affect the sealing of packaging materials negatively when present on the surface of the sealing layer in a high amount. Consequently, in the case of a multilayer film wound in a reel, there would never be the formation of primary amines, but only (poly)urea, as schematically depicted in [Figure 1b](#). However, if the same multilayer material were used shortly after lamination to pack a high a_w food, PAAs would be solubilized in the surrounding moisture as soon as they get formed, with consequent diffusion from the internal surface of the laminate to the interior of the package, i.e. to the food. In compliance with the quality management procedures for good manufacturing practice for materials and articles intended to come into contact with food (regulation 2023/2006) ([European Commission, 2006](#)), laminate manufacturers (e.g., the *converters*) define experimentally (e.g., spectrophotometrically) for each multilayer system the time necessary after lamination to achieve the complete migration of the isocyanic monomer, i.e. the time after which the formation of PAAs no longer occurs (this time is often called *PAAs decay*). Such a time span, which is assumed as the minimum time required before using the packaging material in a safe way, depends on many variables, such as the environmental conditions (e.g., temperature), the PU adhesive system (e.g., type of isocyanic, polyol component, amount of free isocyanic monomer, presence of catalysts, chain extenders, etc.), and the plastic layer between the adhesive and the food matrix (e.g. type of polymer, film thickness, presence of additives such as plasticizer, etc.) ([Wirts, Grunwald, Schulze, Uhde, & Salthammer, 2003](#)). Therefore, there will reasonably be a specific PAAs decay for each specific packaging system.

As demonstrated by our literature survey, much less attention has been paid so far to the potential formation of PAAs from alternative routes (e.g., secondary reactions) that, although being quantitatively less significant than the main pathway seen before, could lead to exceed the maximum concentration of PAAs allowed by the current regulations on packaging materials intended to come in contact with food.

This article specifically focuses on the formation of PAAs arising from the cleavage of secondary bonds (namely allophanate and biuret bonds) on the main PU backbone due to the effect

of high temperatures. Such high temperatures can be due to both typical preservative thermal treatments (e.g., pasteurization and sterilization) and pre-consumption operations (e.g., vacuum-cooking, microwaving, etc.) on packaged foods. However, because greater attention is generally posed to the “in service” life of packaged food, we deliberately focused on the heat treatments occurring before the food reaches the market shelves. After highlighting the chemical basis of the PAAs formation, we describe the physical aspects associated with their migration, in order to better clarify the potential risks that might arise from an underestimation of the overall phenomenon. The purpose of this viewpoint article is to draw attention to an aspect that has not been fairly considered over the past years. Towards this goal, we have stressed the importance of strictly complying with the current legislation on food contact materials through an adequate setting of the assessment procedures for the quantification of PAAs migrating from the packaging to the food after thermal treatments.

Fundamental chemistry underlying the formation of primary aromatic amines (PAAs)

The isocyanic group ($-NCO$) can react with a number of compounds containing free functional groups with mobile hydrogen atoms. The reactivity depends on the characteristics of the functional group, as summarized in [Table 1](#). As mentioned in the previous section, the reaction between an isocyanic group and a hydroxyl group has long since been exploited to obtain the urethane linkage. In particular, PU adhesive systems are mainly obtained using aromatic di-isocyanates, the most widely used being methylene diphenyl diisocyanate (MDI) and toluene diisocyanate (TDI) ([Meier-Westhues, 2007](#)). In the presence of water, the reaction to an aromatic isocyanic group leads to the formation of an aromatic amine, with carbamic acid as an instable intermediate and CO_2 as a side product.

While the amines formation is immediately followed by the formation of (poly)ureas through an immediate reaction with the next migrating isocyanic monomer in multi-layer flexible films wound in a reel, a potential safety issue may occur when the same materials are in service. As explained before, the problem is practically overcome by proper handling of the laminates, i.e., by the

assessment of the minimum time needed to allow complete migration of the isocyanic monomer from the adhesive layer to the surface that will come into contact with the food. However, this approach only accounts for the potential risk associated with the unreacted isocyanic monomers, thus neglecting any neo-formed PAAs possibly arising from post-treatments of packaged foods. Thermal treatments on packaged foods find applications as a method of cooking, e.g., in vacuum cooking and microwave ovens. However, heat treatments are most often used in the food industry to preserve the packaged foods from microbial spoilage and contamination, thus extending the shelf life. This is achieved through a proper setting of the temperature and the time of the thermal treatment. While pasteurization aims to control the microbial growth with light thermal treatments (e.g., 90°C for 60 minutes), sterilization aims to kill all micro-organisms in the food with the combined use of high temperatures and pressures for a specific amount of time. Typical conditions are 121 °C × 30 minutes or 134 °C × 3 minutes (Lee, Yam, & Piergiovanni, 2008)

Because the binding energy of the urethane bond can withstand these conditions, the cleavage of this linkage due to preservative thermal treatments has to be excluded (Fabris, 1976; Szycher, 2012). It is likely that there may be some chemical breakdown of the main polymeric chain (depolymerization), with the consequent formation of chains with a lower molecular weight, but in any case, not low enough to allow their migration (Yang, Macosko, & Wellinghoff, 1986). Conversely, these thermal treatments may disrupt some secondary bonds displaced on the main PU backbone, such as allophanate and biuret bonds (Fedseev, Marchenko, & Rogov, 1973; Griffin & Willwerth, 1962; Kogon, 1959). Allophanates and biurets are formed after addition-type reactions between isocyanic monomers and urethane and ureic groups, respectively. (Figure 2, schemes 3 and 4). The amount of allophanate and biuret bonds found in a PU adhesive polymer chain depends, among other factors, on the reaction molar ratio between the polyisocyanic component and polyol component—that is, the higher the amount (in moles) of polyisocyanate, the higher the amount of the above bonds formed (Dušek, Ilavský, & Matějka, 1984). In addition, the polymerization temperature may affect the formation of allophanate and biuret bonds, because higher temperatures will lead to a

greater formation of allophanate and biuret linkages. On the other hand, the presence of the catalyst and its concentration can also influence the amount of these linkages, reducing the required temperature for their formation (Lapprand, Boisson, Delolme, Méchin, & Pascault, 2005).

Due to the higher amount of urethane groups compared to the ureic ones, the allophanate bonds exceed the biuret ones on the main PU adhesive backbone. As shown in Table 2, the thermostability of the above linkages follows the order: urea > urethane > biuret > allophanate. In addition, among allophanate bonds, those obtained from aromatic isocyanic monomers are thermally less stable than those obtained from aliphatic isocyanic monomers (see Table 2). As a consequence, the low thermal stability of allophanates and, to a lesser extent, biurets, can be indicated as the main cause of “re-formation” of isocyanic monomers when laminate structures obtained with aromatic polyurethane adhesive systems are used. The cleavage of the allophanate and biuret bonds begins at approximately 70 °C, and the rate of the “re-formation” of the monomer increases with an increase in temperature, until it can be considered complete for temperatures above 105 °C (Kogon, 1958, 1959; Yoshitake & Furukawa, 1995).

When a multilayer packaging system obtained using a polyurethane adhesive is subjected to a preservative thermal cycle, there will always be the re-formation of isocyanic monomers due to the cleavage of allophanate linkages as a result of the thermal energy input and the duration of the heating process (Figure 3a). It should also be noted that the migration of the newly formed isocyanic monomer is not so unlikely, due to two main reasons: i) the low molecular weight (MW) of isocyanates, especially when TDI (MW = 174.2 g mol⁻¹) and MDI (MW = 250.5 g mol⁻¹) are used; and ii) the increased relaxation of the molecular chains of the inner plastic layer (i.e., the sealing layer, which is most often a polyolefin such as low-density polyethylene, LDPE or cast polypropylene, C-PP) due to the high temperature used, which is well above the glass transition temperature (T_g LDPE ~ -125 °C) and, in some circumstances, close to the melting temperature of the polymer (T_m LDPE ~ 105–125 °C) (Malpass, 2010).

As anticipated in the previous section, the potential re-formation of isocyanic monomers becomes a crucial point for liquid foods (e.g., retort pouches containing soups) or high water activity (a_w) foods. In fact, when the isocyanic monomers encounter water molecules, the formation of PAAs readily occurs due to the high reactivity of the $-NCO$ group to water at the preservative thermal cycle temperature (Avar, Meier-Westhues, Casselmann, & Achten, 2012). Provided that the above chemical pathway will find experimental evidence, PAAs can be classified as non-intentionally added substances (NIAS). In addition, because the internal moisture of the package contributes to washing out the freshly formed PAAs from the inner surface of the package (i.e., the sealing layer), the migration of the isocyanic monomers will continuously take place as long as they are consumed through the PAAs formation. In other words, the internal moisture triggers the formation of PAAs, which will thus migrate continuously from the inner packaging layer to the food matrix (Figure 3b).

The most effective counteraction to tackle this issue would be not to use the aromatic isocyanates as starting molecules in the adhesive formulation. However, the use of aliphatic adhesive systems is generally deemed unprofitable. This is because first of all, aliphatic adhesive systems are more costly than polyurethane adhesive systems exclusively based on aromatic isocyanates (aromatic adhesive systems). Secondly, aliphatic adhesive systems have a much lower reactivity compared to the aromatic ones (Chattopadhyay & Radju, 2007). The low reactivity of aliphatic adhesive systems forces converters to extend the storage time of the multilayer reels in the climatic rooms in order to guarantee an adequate degree of polymerization that, in turn, will dramatically affect the ultimate sealing and thermal performance of the PU adhesive. Therefore, the use of aliphatic isocyanates may negatively impact the overall throughput due to evident logistic problems. For all those applications, envisaging the use of aromatic adhesive systems, an assessment of the risk associated with the formation of PAAs “post-thermal treatments” (i.e., after subjecting the packaging materials to preservative thermal cycles) is of utmost importance. Actually, the ongoing European legislation on food contact materials (regulation 10/2011) provides clear provisions for the migration tests on food packaging materials subjected to thermal treatments, inspired by the basic principle that “...the risk

assessment should cover the potential migration under worst foreseeable conditions of use and the toxicity” (European Commission, 2011). Accordingly, assuming a thermal cycle between 121 °C and 130 °C × 0.5 to 1 hour, the migration test should be carried out at 130 °C × 1 hour using the simulant B (water solution of acetic acid 3%, w/v). As confirmed by the work of Pezo and co-workers, the conditions set out by the legislation guarantee a reliable quantification of the PAAs possibly formed after the thermal treatment (Pezo *et al.*, 2012). The main question thus becomes: Do converters take care of quantifying the neo-formed PAAs possibly coming from the preservative thermal treatments of liquid/high a_w foods? Based on an informal survey we conducted throughout the year 2014, out of 52 companies (20 located in Italy, 32 across the European Union), only five (i.e. less than 10%) declared that they consciously complied with the current legislation. This means that they performed the quantification of PAAs accounting for any “*worst foreseeable conditions,*” possibly occurring from lamination to service, namely, also considering the preservative thermal cycles (e.g., pasteurization and sterilization). The remaining “outlaw” companies (which of course will be kept undisclosed), though aware of the existence of a specific legislation, admitted to do what many companies do: only quantify the PAAs decay time after lamination. Although the sample we considered cannot be considered as an absolute depiction of the facts, and we cannot generalize the outcome of our survey, it is, however, indicative of a potential scenario among converters. The seriousness of this matter imposes a careful consideration of the risks for public health associated with a potential underestimation of PAAs that may contaminate some types of packaged food. On the other hand, all of the interviewed subjects stated that the quantification of PAAs (both “pre-thermal treatments” and “post-thermal treatments”) is performed by the spectrophotometric method (which is in accordance with the requirements of Article 11 of regulation 882/2004 of the European Commission), as equivalent to aniline, probably because it represents a user-friendly, low-cost, and time saving approach compared to most sophisticated and complex techniques (e.g., chromatography analyses). However, it has been pointed out that this colorimetric method is not selective and can overestimate the total amount of PAAs (Aznar *et al.*, 2009; Brede *et al.*, 2003; Pezo *et al.*, 2012).

Therefore, in addition to a greater sensibility of all stakeholders (from the converters to the surveillance authorities) to prevent consumers from potential contamination of foods due to the migration of PAAs above the legislation limits, new easy-to-use, cost-effective, and accurate analytical methods should take over as mandatory procedures for a reliable assessment of the PAAs that migrated from the package to the food. This appears in accordance with the same regulation 10/2011 of the European Commission (forward 45), which clearly states, “Certain migration testing rules should be updated in view of new scientific knowledge. Enforcement authorities and industry need to adapt their current testing regime to these updated rules [...]” ([European Commission, 2011](#)).

Conclusions

The migration of primary aromatic amines from food-packaging materials represents a serious risk to public health as PAAs are potentially carcinogenic substances. Although the main source of PAAs is represented by residues of aromatic isocyanates arising from incomplete curing of the main polyurethane adhesive, the thermal effect of heat treatments from ~ 70 °C on, both before reaching the market (e.g., preservative thermal treatments) and after being put in service (e.g., vacuum cooking), may contribute to a significant increase of PAAs migrating into the food. This is the crucial point: Who, among the stakeholders (especially converters), really knows about the potential formation of PAAs possibly caused by thermal treatments on packaged foods, especially before going to the market shelves? The risk is that without this knowledge, the worst foreseeable conditions will not be properly set, leading to a consequent underestimation of the PAAs possibly reaching the food. Based on our experience, the interpretation of the legislation by converters is often wrong, as they tend to consider the “*worst foreseeable conditions*” as only those occurring after the packaged food has been placed on the shelves. However, the legislation indeed includes all the treatments that the package may experience before it enters the market. As long as this aspect remains not totally understood, the risks for public health associated with a potential migration of PAAs that may contaminate some types of packaged food will be high.

At the same time, an “updating” of the analytical tools is necessary for a reliable quantification of PAAs possibly migrating from the packaging materials to the food. In particular, the spectrophotometric/colorimetric method (as equivalent to aniline) does not seem to provide accurate results compared to, for example, chromatography techniques, which are, however, more complicated and expensive, and thus less willingly adopted by most converters.

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Figure captions

Figure 1. (a) Schematic representation of a PU adhesive-based laminate packaging material (3-layer structure). (b) Sketch on the formation of poly(urea) in PU adhesive-based multilayer packaging materials wound in reels. Red-white spheres: water molecules; Ar-NCO: aromatic isocyanate monomers; Ar-NH₂: aromatic amines.

Figure 2. Schematic reaction mechanisms between: an isocyanic group and a hydroxyl group for the formation of an urethane linkage (scheme 1); an isocyanic monomer and a water molecule to yield a primary amine (scheme 2a); a primary amine and an isocyanic monomer to yield an urea (scheme 2b); an urethane group and an isocyanic monomer leading to an allophanate linkage (scheme 3); and an ureic group and an isocyanic monomer to yield a biuret linkage (scheme 4).

Figure 3. (a) Illustrative drawing of the formation of the isocyanic monomer from the thermal cleavage of the allophanate linkage. (b) Rendering image representing the potential migration of PAAs from the packaging to the food matrix. Red-white spheres: water molecules; black-blue spheres: representative aromatic amine; yellow arrows: migration of the isocyanic monomer; cyan arrows: washing-out effect of environmental moisture.

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Figure 1

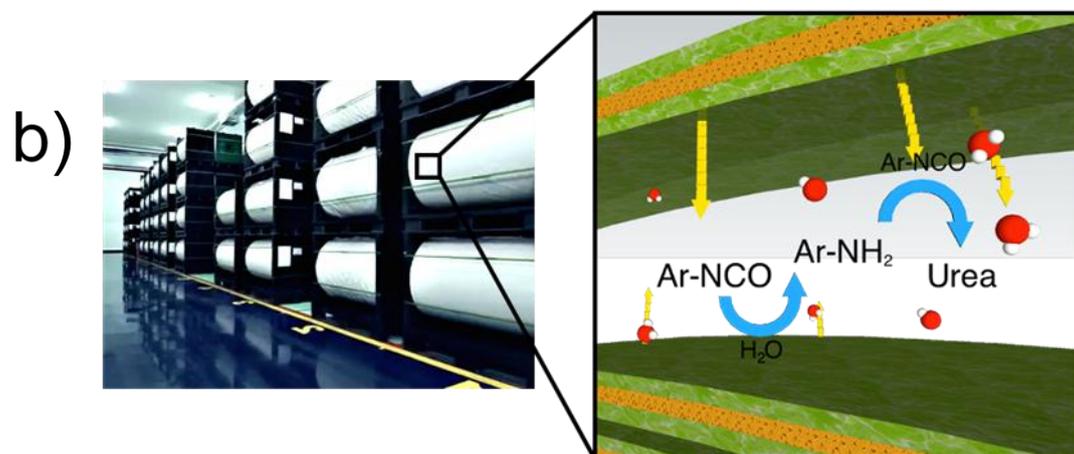
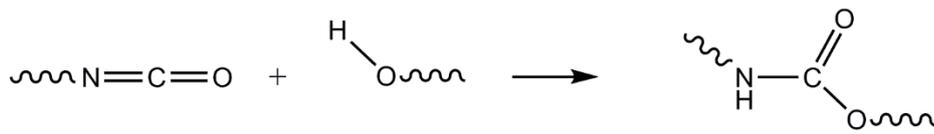
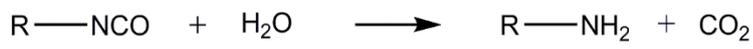


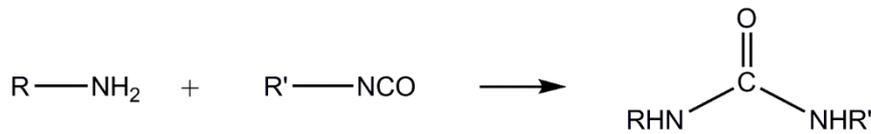
Figure 2



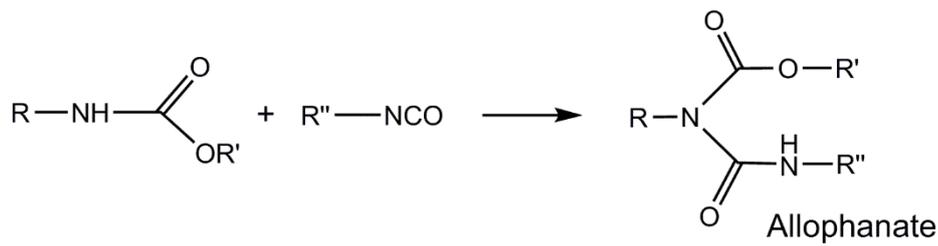
scheme 1



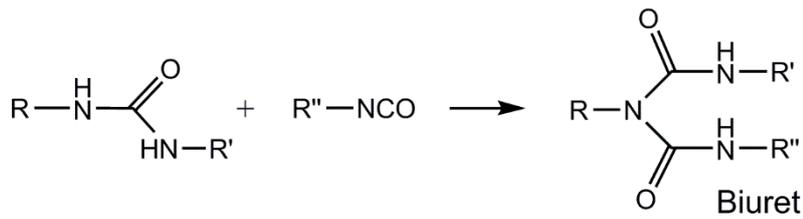
scheme 2a



scheme 2b



scheme 3



scheme 4

Figure 3

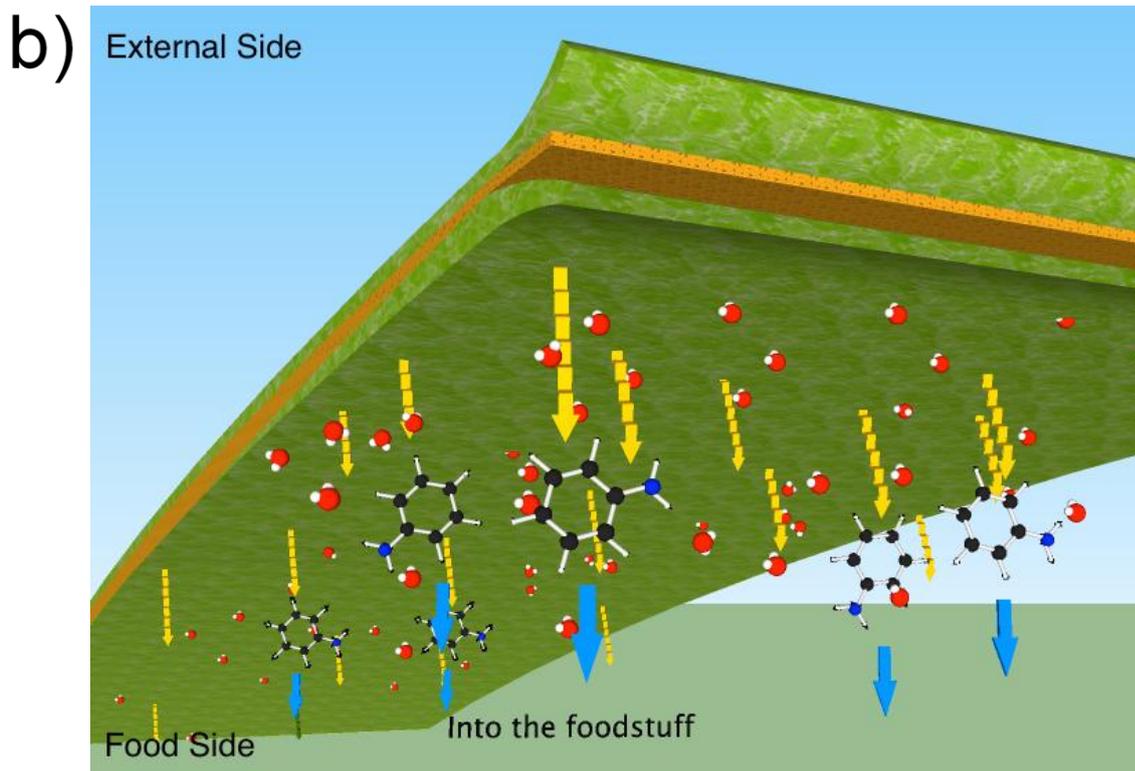
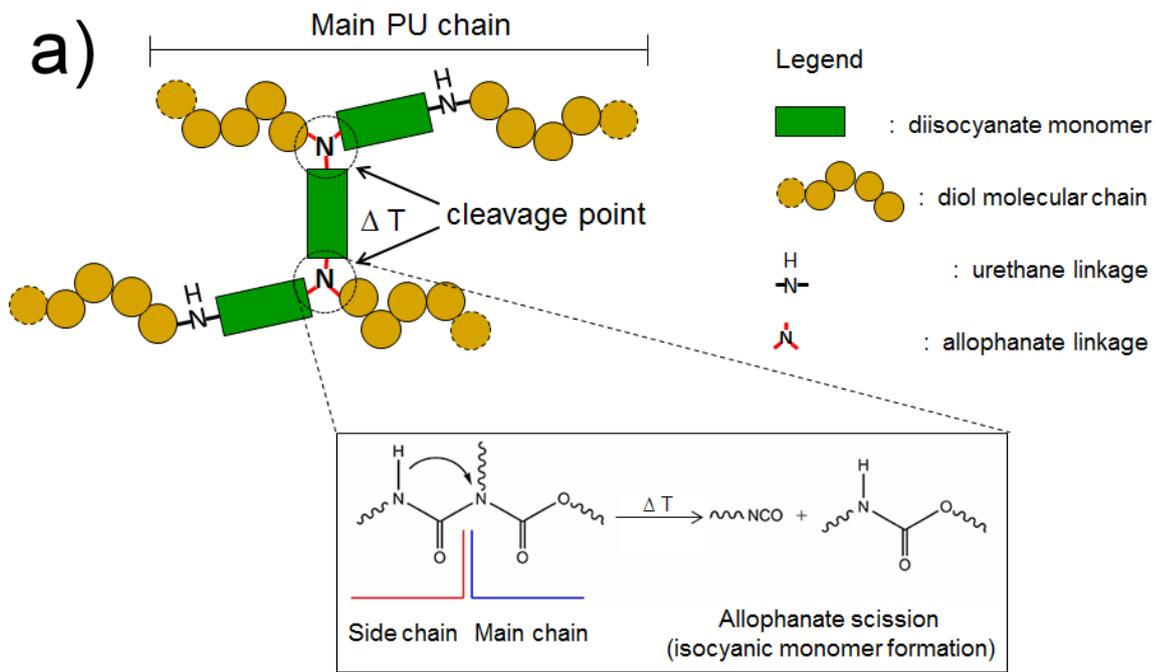


Table 1. Relative reactivity of active hydrogen compounds against isocyanate (data normalized according to the rate of the isocyanate/water reaction, adapted from Ionescu, 2005).

Hydrogen Active Compound	Formula	Relative Reactivity Rate (non-catalyzed, 25 °C)
primary aliphatic amine	R-NH ₂	1000
secondary aliphatic amine	R ₂ -NH	200-500
primary aromatic amine	Ar-NH ₂	2-3
primary hydroxyl	RCH ₂ -OH	1
water	H ₂ O	1
secondary hydroxyl	R ₂ CH-OH	0.3
urea	R-NH-CO-NH-R	0.15
tertiary hydroxyl	R ₃ C-OH	0.005
phenolic hydroxyl	Ar-OH	0.001-0.005
urethane	R-NH-COOR	0.001

Table 2. Thermal dissociation temperatures of linkages found in polyurethanes (adapted from Delebecq, Pascault, Boutevin, & Lyon, 2013; Lapprand, Boisson, Delolme, Méchin, & Pascault, 2005; Ionescu, 2005).

Linkage	Onset of dissociation (°C)
Aromatic urethane ^a	~ 200
Aliphatic urethane ^b	~ 250
Aromatic urea	140-180
Aliphatic urea	160-200
Aromatic biuret	100-110
Aliphatic biuret	115-125
Aromatic allophanate	85-105
Aliphatic allophanate	100-120
Disubstituted urea	235-250

^aFormed by reaction between an aryl isocyanate and an alkyl alcohol

^bFormed by reaction between an alkyl isocyanate and an alkyl alcohol

Highlights

- Primary aromatic amines (PAAs) can be found in multilayer packaging materials.
- The origin of PAAs in polyurethane adhesive-based multilayer packages is here discussed.
- We propose the neo-formation of PAAs from the thermal cleavage of allophanate linkages.
- Provisions included in the current European legislation are reported.
- The need for more sophisticated analytical tools is stressed.