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Amino Acid Catalysis of 2-Alkylfuran Formation from Lipid Oxidation-Derived α,β-Unsaturated Aldehydes

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ABSTRACT: The formation of 2-alkylfurans from the corresponding lipid-derived α,β-unsaturated aldehydes under dry-roasting conditions was investigated in detail. The addition of an amino acid to an α,β-unsaturated aldehyde drastically increased 2-alkylfuran formation. Peptides and proteins as well were able to catalyze 2-alkylfuran formation from the corresponding α,β-unsaturated aldehydes. Further investigation of 2-alkylfuran formation showed the need of oxidizing conditions and the involvement of radicals in the reaction. This way, the formation of 2-methylfuran from 2-pentenal, 2-ethylfuran from 2-hexenal, 2-propylfuran from 2-heptenal, 2-butylfuran from 2-octenal, 2-pentylfuran from 2-nonenal, and 2-hexylfuran from 2-decenal was shown. The impact of amino acids on 2-alkylfuran formation from lipid-derived α,β-unsaturated aldehydes represents an interesting example of the complex role of amino acids in the multitude of chemical reactions occurring during thermal processing of lipid-rich foods.

KEYWORDS: 2-Alkylfurans, lipid oxidation, amino acids, α,β-unsaturated aldehydes

INTRODUCTION

Two of the most important reactions responsible for the development of flavor in processed foods are the Maillard reaction between carbohydrates and amino acids, on the one hand, and lipid degradation, on the other hand. In food, however, both reactions are closely related: Lipid oxidation products or intermediates can influence the course of the Maillard reaction and vice versa. Specific carbonyl compounds and heterocyclic aroma compounds can result from both reaction pathways.[1,2]

Furans are among the most ubiquitous heterocyclic compounds in thermally processed foods.[3,4] Carbohydrates (in the presence or absence of amino acids) are primary sources of furans in food, for instance, furfural, 2-acetylfuran, and 2-methylfuran. 2-Alkylfurans, especially those with longer alkyl side chains, mainly result from the degradation of lipids, and are common among the flavor volatiles of, for example, meat products and coffee.[3] In this respect, 2-alkylfurans are sometimes mentioned as markers of lipid oxidation. 2-Pentylfuran, for instance, is commonly reported as an oxidation product of linoleic acid and possesses a buttery flavor, resembling green beans.[5] 2-Ethylfuran, evoking a powerful burnt, sweet, coffeelike flavor,[3] has also been suggested to represent the extent of lipid oxidation in food systems, for example, in cod liver oil and cooked salmon.[6,7]

Secondary lipid oxidation products, in particular 4-hydroxy-2-alkenals, are probable precursors of 2-alkylfurans in foods, but the mechanism involved is poorly described in the literature. Cyclization of a 4-hydroxy-2-alkenal followed by dehydration can yield the corresponding 2-alkylfuran. α,β-Unsaturated aldehydes, however, are potential precursors of 2-alkylfurans as well. Quantitatively, these 2-alkenals are more important than the corresponding 4-hydroxy-2-alkenals in food products.[8] Grein et al.[9] described the water-mediated oxidative decomposition of α,β-unsaturated aldehydes (0.02 M concentration of aldehydes, pH 6.5, room temperature). They reported the formation of 4-hydroxy-(*E*)-2-hexenal from (*E*)-2-hexenal and of 4-hydroxy-(*E*)-2-octenal from (*E*)-2-octenal as minor compounds, but the corresponding 2-alkylfurans were not detected. From (*E*,*E*)-2,4-decadienal, (*E*)-4,5-epoxy-2-decenal was formed, but in addition, 4-hydroxy-2-nonenal and 2-pentylfuran were identified. The authors postulated an allylic hydroperoxidation for the formation of 4-oxygenated compounds, possibly cyclizing toward the corresponding 2-alkylfurans.

In our previous research, we studied the formation of volatile[10] and nonvolatile[11] reaction products of amino acids with various lipid oxidation products, in comparison with Maillard reaction systems. As we observed that amino acids were efficient catalysts of the formation of 2-alkylfurans from the corresponding α,β-unsaturated aldehydes,[10] we studied this reaction in detail. The impact of amino acids on 2-alkylfuran formation from lipid-derived α,β-unsaturated aldehydes may represent an interesting example of Maillard type carbonyl−amine interactions occurring in lipid-rich foods. The reaction mechanism of 2-alkylfuran formation from α,β-unsaturated aldehydes and amino acids requires, therefore, further attention.

MATERIALS AND METHODS

Chemicals. Alanine (99%), glutamic acid (99%), arginine monohydrate (98%), lysine monohydrate (99%), methionine (98%), (*E*)-2-pentenal (97%), (*E*)-2-hexenal (99%), (*E*)-2-heptenal (97%), (*E*)-2-decenal (95%), 2-ethylfuran (99%), L-(+)-ascorbic acid (99%), sodium bisulfite, copper(II)chloride, iron(III)chloride, butylated hydroxyanisole (BHA, 96%), and azobisisobutyronitril (AIBN, 98%) were from Acros Organics (Geel, Belgium). Glycine (99%), aspartic acid (98%), glutamine (98%), threonine (98%), histidine (98%), leucine (99%), diglycine (>99%), triglycine, tetraglycine, casein, (*E*)-2-octenal (94%),

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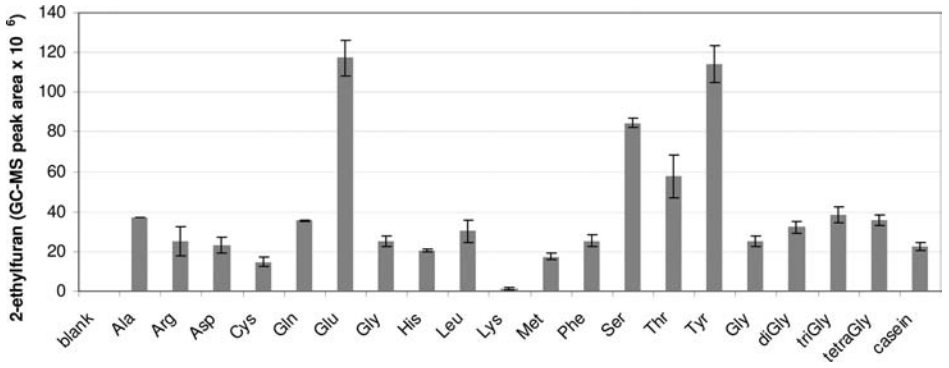


Figure 1. Influence of the addition of various amino acids, peptides, and casein (2 equiv) on the formation of 2-ethylfuran from (*E*)-2-hexenal under dry-roasting conditions (180 °C, 20 min), as measured by SPME-GC-MS peak area. Values are means of three repetitions with standard deviations as error bars. Blank refers to only (*E*)-2-hexenal. 2-Ethylfuran was not detected in case of addition of proline, benzylamine, and dibenzylamine.

(*E*)-2-nonenal (97%), and ^{18}O-labeled water (Isotec, 97% ^{18}O atoms) were from Sigma-Aldrich (Bornem, Belgium). Serine (99%), phenylalanine (98.5%), and cysteine (97%) were from Janssen Chimica (Geel, Belgium). Tyrosine was from Difco Laboratories (BD, Erembodegem, Belgium). 2-Propylfuran (99%), 2-butylfuran (98%), 2-pentylfuran (98%), and 2-hexylfuran (97%) were from Alfa Aesar (Karlsruhe, Germany).

Model Reactions. For this purpose, 20 mL solid phase microextraction (SPME) vials (Gerstel, Mülheim a/d Ruhr, Germany) were subsequently filled with 0.25 mmol of carbonyl compound, 2 g of sand (purified sea sand, 50−70 mesh, Sigma-Aldrich) and, when required, 0.5 mmol of amino acid (or 1 g of casein) and/or various additives in amounts specified in the tables. The vials were hermetically closed with a magnetic crimp cap with a septum (silicone/PTFE; 55° Shore A; 1.5 mm, Gerstel), mixed well by means of vortex, and placed in an oven (equipped with a fan, Memmert, Schwabach, Germany), which had been preheated to and stabilized at 180 °C. The reaction mixtures were heated for exactly 20 min. After they were heated, the vials were removed from the oven and rapidly cooled in an ice bath. All model reactions were performed in triplicate. To determine the influence of water on the SPME extraction efficiency, authentic standards were analyzed. For this purpose, standard solutions of 2-alkylfurans in methanol (5% v/v) were prepared, and 10 μL of this solution was sprayed on 2 g of sand. To this mixture, varying amounts of water (5−25 μL) or ethanol (10−100 μL) were added, followed by vortex mixing. All standards were prepared in triplicate.

SPME Parameters. SPME extraction and desorption were performed automatically by means of an MPS-2 autosampler (Gerstel). For the analysis of 2-alkylfurans, SPME extraction was performed for 30 min at 35 °C, and desorption took place for 2 min in the hot GC inlet (250 °C). A divinylbenzene/Carboxen/polydimethylsiloxane (DVB/Carboxen/PDMS) fiber (Supelco, Bornem, Belgium) was used.

Desorption of blank 2-alkenal mixtures at three different temperatures (230, 250, and 270 °C) showed the formation of traces of the corresponding 2-alkylfurans, with no significant difference among the three desorption temperatures. As a result, artifactual formation of 2-alkylfurans on the SPME fiber during fiber desorption (250 °C, 2 min) is negligible.

Mass Spectrometry. For the analysis of volatile reaction products, a Hewlett-Packard 6890 GC Plus coupled with a HP 5973 MSD (Mass Selective Detector-Quadrupole type), equipped with a CIS-4 PTV (Programmed Temperature Vaporization) Injector (Gerstel) and a AT5-MS capillary column (30 mm × 0.25 mm i.d.; coating thickness 0.25 μm) was used. Working conditions were as follows: injector, 250 °C; transfer line to MSD, 260 °C; oven temperature, start 40 °C, hold 3 min; programmed from 40 to 200 at 4 °C min^{-1} and from 200 to 240 at 30 °C min^{-1}, hold 2 min; split ratio, 10:1; carrier gas (He), 1.2 mL min^{-1}; ionization EI, 70 eV; and acquisition parameters, scanned m/z 40−200 (0−10 min), 40−300 (10−20 min), and 40−400 (>20 min). Volatile substances were identified by comparison of their mass spectra and retention times with those of reference substances and by comparison with the Wiley (6th ed.) and the NIST Mass Spectral Library (Version 1.6d, 1998).

RESULTS AND DISCUSSION

To study in detail the reaction mechanism of the formation of 2-alkylfurans from the corresponding α,β-unsaturated aldehydes, several model reactions were performed. Model mixtures of an α,β-unsaturated aldehyde, in the presence or absence of various additives, were heated under dry-roasting conditions (180 °C, 20 min). After they were cooled, the headspace of the reaction mixtures was sampled by means of SPME (DVB/Car/PDMS), followed by GC-MS analysis. Results are expressed as GC-MS peak areas and provide as such semiquantitative data. Because of the lack of labeled standards for 2-alkylfurans, reliable quantification by SPME (by means of stable isotope dilution analysis) was unfortunately not possible. Matrix effects were minimized by applying low amounts of precursors in a matrix of sand. By means of automated SPME extraction and desorption, careful control of all of the parameters involved was ensured, and repeatable analyses were accomplished. The relative standard deviation (RSD) of SPME-GC-MS measurements of replicate samples ranged from 2.4% until, occasionally, 48.7% (for compounds present in very low amounts). Analysis of 2-ethylfuran standard mixtures showed a logarithmic response of the SPME-GC-MS peak areas on varying amounts of 2-ethylfuran (data not shown). These standard tests indicated that the analyzed peak areas represent amounts of 2-alkylfurans in the low μmol range.

In the first instance, the formation of 2-ethylfuran from (*E*)-2-hexenal in model systems was investigated. Whereas upon heating of neat (*E*)-2-hexenal no 2-ethylfuran was detected, the addition of an amino acid remarkably increased the formation of 2-ethylfuran (Figure 1). Previous studies showed that aldol type reactions prevailed in model mixtures of unsaturated aldehydes with amino acids.[10] To prevent the prevalence of such (*E*)-2-hexenal self-condensation reactions, 2 equiv of amino acid was applied in the first instance. Later experiments showed, however, that catalytic amounts (0.1 equiv) of the amino acid were sufficient to increase 2-alkylfuran formation (data not shown). In Figure 1, considerable differences in reactivity between the variety of amino acids tested can be noted. The highest amounts of

2-ethylfuran were detected in the presence of glutamic acid and tyrosine, followed by serine and threonine.

The formation of 2-ethylfuran from (*E*)-2-hexenal in the presence of glycine peptides (diglycine, triglycine, and tetraglycine) was significantly higher than from glycine itself. Thus, the addition of peptides and a protein (casein) also enhanced the formation of 2-ethylfuran from (*E*)-2-hexenal. Although the addition of an amino acid has an important influence on 2-alkylfuran formation, it is difficult to distinguish the specific nature of this effect.

When comparing the influence of acidic and basic amino acids on 2-ethylfuran formation, no clear trend could be observed: Whereas the addition of glutamic acid induced the highest 2-ethylfuran formation, the formation of 2-ethylfuran in the presence of aspartic acid was much lower (Figure 1). In the presence of lysine, the 2-ethylfuran peak was very low, while tyrosine increased 2-ethylfuran formation, although both side chains have a similar pK_a (around 10). Thus, acid/base catalysis by the amino acid side chain is most probably not responsible for the increase in 2-alkylfuran formation upon addition of an amino acid.

If increased cyclization toward the 2-alkylfuran would be due to the formation of an imine in a first step, a secondary amine would be more advantageous than a primary amine. However, in the presence of proline, no 2-ethylfuran was detected upon heating of (*E*)-2-hexenal (data not shown). In the presence of benzylamine, only traces of 2-ethylfuran were found, while no 2-ethylfuran was detected in the presence of dibenzylamine (data not shown). Moreover, low amounts of 2-ethylfuran were noted in case of lysine, having a very reactive ε-amino group. These results imply that the formation of an imine prior to cyclization cannot explain the positive effect of the amino acids on 2-alkylfuran formation. Conversely, those amino compounds expected to be more prone to imine formation showed very low yields of 2-ethylfuran. As the Strecker aldehyde phenylacetaldehyde was not detected in the phenylalanine model systems, Strecker degradation does not occur to a considerable extent. This indicates again that imine formation is probably not a key step in the reaction mechanism.

The addition of an amino acid, peptide, or protein to the α,β-unsaturated aldehyde induced browning and enhanced the general reaction rate in the model systems. The 2-alkylfurans were actually minor compounds in a complex reaction mixture. An overview of the different reaction products of these model systems, among which are 2-alkylfurans, has been discussed elsewhere.[10] Measurement of the degree of browning of the model systems, however, showed no correlation between browning and 2-ethylfuran formation: In some cases, a high extent of browning was accompanied with low amounts of 2-ethylfuran and vice versa.

To identify important parameters in the formation of 2-alkylfurans from the corresponding α,β-unsaturated aldehydes, the cyclizations of (*E*)-2-hexenal to 2-ethylfuran and of (*E*)-2-heptenal to 2-propylfuran were investigated under different reaction conditions, in the presence of phenylalanine. Phenylalanine was selected as model amino acid, as it had an intermediate effect on 2-alkylfuran formation among the amino acids tested. In addition, phenylalanine degradation products, such as the Strecker aldehyde phenylacetaldehyde, are easily detectable by means of gas chromatography and may be an indication of specific reaction mechanisms that occur. The resulting GC peak areas of the 2-alkylfurans are displayed in Table 1.

It must be noted that, in the absence of an amino acid, no 2-ethylfuran was detected for almost all reaction conditions evaluated

Table 1. Formation of 2-Ethylfuran from (*E*)-2-Hexenal and of 2-Propylfuran from (*E*)-2-Heptenal in the Presence of 2 equiv of Phenylalanine under Dry-Roasting Conditions (180 °C, 20 min), as Measured by SPME-GC-MS Peak Area (×10^6)

additives	2-ethylfuran	2-propylfuran
2-alkenal not heated	31.43 ± 3.88 a[a]	7.44 ± 3.70 a
2-alkenal	43.89 ± 3.85 c	89.41 ± 9.41 b
+ 5 μL of water	68.48 ± 6.69 d	NA[b]
+ 15 μL of water	87.40 ± 10.53 e	153.43 ± 13.93 c
+ 25 μL of water	115.03 ± 13.75 f	NA
+ 15 μL of 2 N NaOH	34.04 ± 5.26 a	129.53 ± 23.94 c
+ 15 μL of 2 N HCl	78.76 ± 22.10 e	252.90 ± 38.70 d
+ N_2 atm	11.39 ± 1.87 g	11.49 ± 0.89 a
+ 0.01 equiv of vit C in 15 μL of water	91.40 ± 8.55 e	177.75 ± 10.81 c
+ 1 equiv of $NaHSO_3$	24.92 ± 0.66 b	110.11 ± 6.60 e
+ 1 equiv of $NaHSO_3$ in 15 μL of water	29.00 ± 6.82 ab	111.34 ± 15.27 e
+ 15 μL of 2 M $CuCl_2$	295.62 ± 38.68 h	359.36 ± 43.90 f
+ 10 μL of EtOH	29.02 ± 9.53 abi	62.05 ± 8.84 g
+ 10 μL of 0.1 M BHA in EtOH	27.16 ± 2.21 ab	96.06 ± 14.23 b
+ 100 μL of EtOH	15.01 ± 1.99 i	NA
+ 100 μL of 0.01 M AIBN in EtOH	321.18 ± 119.01 h	294.10 ± 143.13 df[c]

[a] Different letters within one column indicate significant differences ($\alpha = 0.05$). [b] NA, not analyzed. [c] In 10 μL of ethanol.

(except in the presence of 100 μL of ethanol and with NaOH). On the contrary, 2-propylfuran was detected upon heating of (*E*)-2-heptenal in most cases (except in the nonheated sample and in the presence of sodium bisulfite); the resulting peak areas remained a factor 3−10 lower than in the presence of phenylalanine.

At first, the effects of heating and of the addition of small amounts of water to the dry model system were evaluated. The addition of phenylalanine seemed sufficient to catalyze the formation of 2-ethylfuran and 2-propylfuran from the corresponding α,β-unsaturated aldehydes, even without heating. Heating the model systems (180 °C, 20 min) significantly increased 2-alkylfuran formation. The addition of small amounts of water (0−25 μL) additionally increased 2-alkylfuran formation upon heating. The 2-ethylfuran peak area increased linearly with the amounts of water added ($R^2 = 0.976$). Standard tests analyzing 2-ethylfuran (5 μmol) in the presence of increasing amounts of water (0−25 μL) showed that this effect was partly due to an enhanced SPME extraction of 2-ethylfuran in the presence of small amounts of water (data not shown). This can be attributed to an increased expulsion of 2-ethylfuran to the headspace. On the basis of the slopes of the fitted straight lines, however, the increase in 2-ethylfuran formation upon heating was almost three times higher than the corresponding increase in SPME extraction efficiency caused by the addition of water. Therefore, it can be stated that the presence of water effectively increased 2-ethylfuran formation. As the addition of ^{18}O-labeled water showed no incorporation of the ^{18}O-label in 2-ethylfuran, water does not take part in the reaction as a hydroxylating reagent itself. Probably, the effect of water is merely due to an increased mobility of the reagents.

To elucidate the effect of acid/base catalysis further, the addition of an acidic (2 N HCl) and an alkaline solution

Scheme 1. Hypothesized Reaction Mechanism for the Formation of 2-Alkylfuran from the Corresponding (*E*)-2-Alkenal

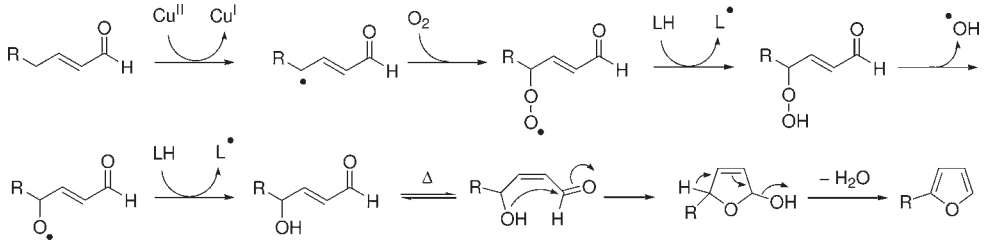


Table 2. Formation of the Corresponding Substituted Furans from α,β-Unsaturated Aldehydes in the Absence and Presence of 2 equiv of Phenylalanine under Dry-Roasting Conditions (180 °C, 20 min), as Measured by SPME-GC-MS peak Area (×10^6)

	carbonyl	without Phe + water[a]	+ 2 M $CuCl_2$[a]	carbonyl	with Phe + water[a]	+ 2 M $CuCl_2$[a]
2-methylfuran from 2-pentenal	2.90 ± 0.71 a[b]	ND[c]	2.21 ± 0.59 a	6.05 ± 0.96 b	6.84 ± 2.92 b	20.86 ± 2.82 c
2-ethylfuran from (*E*)-2-hexenal	ND	ND	ND	43.89 ± 3.85 a	87.40 ± 10.53 b	295.62 ± 38.68 c
2-propylfuran from (*E*)-2-heptenal	11.51 ± 1.78 a	15.42 ± 3.06 a	52.37 ± 10.41 b	89.41 ± 9.41 c	153.43 ± 13.93 d	359.36 ± 43.90 e
2-butylfuran from (*E*)-2-octenal	ND	ND	77.10 ± 3.23 a	ND	67.24 ± 10.08 a	513.63 ± 19.50 b
2-pentylfuran from (*E*)-2-nonenal	7.61 ± 0.50 a	13.89 ± 5.48 a	73.36 ± 4.96 b	137.93 ± 5.50 c	260.10 ± 6.32 d	465.70 ± 128.57 e
2-hexylfuran from (*E*)-2-decenal	11.70 ± 1.49 a	19.01 ± 0.84 b	55.07 ± 7.08 c	46.23 ± 2.63 c	151.47 ± 14.10 d	481.08 ± 122.26 e

[a] 15 μL. [b] Different letters within one row indicate significant differences ($\alpha = 0.05$). [c] ND, not detected.

(2 N NaOH) was investigated. As already suggested from the various amino acids applied, these results were also inconclusive: In the case of (*E*)-2-hexenal, the addition of an alkaline solution decreased 2-ethylfuran formation, while the addition of an acid solution did not have a significant effect (Table 1). From (*E*)-2-heptenal on the other hand, more 2-propylfuran was formed in case of acid catalysis, whereas alkaline catalysis did not show a significant influence.

To be able to cyclize into the corresponding 2-alkylfuran, hydroxylation in the γ-position of the carbonyl group of the α,β-unsaturated aldehyde is required, followed by isomerization of the double bond from the *E* to the *Z* configuration. The intermediate 4-hydroxy-2-alkenals formed are known as very reactive compounds. Especially 4-hydroxy-2-hexenal and 4-hydroxy-2-nonenal are described as highly toxic lipid oxidation-derived compounds, reacting readily with proteins and aminophospholipids under physiological conditions.[12] However, their formation from the corresponding α,β-unsaturated aldehydes is not described in literature.

Considering the oxidative nature of the mechanism of 2-alkylfuran formation proposed in Scheme 1, the effect of various oxidizing and reducing agents was investigated. Performing the reaction under inert nitrogen atmosphere induced a very significant reduction in 2-alkylfuran formation, thus suggesting the importance of oxygen in the oxidation step (Table 1). The addition of the food-grade antioxidant vitamin C (in low amounts) did not significantly change the 2-alkylfuran peak areas. The reducing agent sodium bisulfite significantly reduced 2-alkylfuran formation, in dry and aqueous conditions (as compared to the corresponding model systems not containing sodium bisulfite), although an unexpected small increase in the 2-propylfuran peak area was observed upon the addition of sodium bisulfite to 2-heptenal. Besides, as a reducing agent, bisulfite is known to stabilize imines and may thus have a dual effect in the model reactions.[13,14]

The addition of an aqueous oxidizing $CuCl_2$ solution strongly increased 2-alkylfuran formation. The combination of these results clearly shows the importance of oxidative reaction conditions in an efficient formation of 2-alkylfurans from the corresponding α,β-unsaturated aldehydes. Because of the strong catalytic effect of copper ions in 2-alkylfuran formation, it cannot be excluded that varying levels of trace metals in the amino acid reagents are partly responsible for the varying influence of the amino acids noted.

The importance of radicals in the mechanism was evaluated by means of the addition of a radical scavenger butylated hydroxyanisole (BHA) and a radical initiator azobisisobutyronitrile (AIBN), as ethanolic solutions. The effect of BHA was small and not clear: 2-Ethylfuran formation was not significantly influenced, while 2-propylfuran formation showed a slight increase. The addition of AIBN clearly enhanced the formation of the respective 2-alkylfurans, although the variability on the results obtained was quite high. Thus, the oxidation mechanism probably follows a radical pathway.

Following the same reaction mechanism, the formation of 2-methylfuran from (*E*)-2-pentenal, 2-butylfuran from (*E*)-2-octenal, 2-pentylfuran from (*E*)-2-nonenal, and 2-hexylfuran from (*E*)-2-decenal was shown (Table 2). It must be noted that quantitative comparison of GC peak areas obtained for different 2-alkylfurans is not relevant, as each compound shows a different response for SPME extraction. Analysis by means of SPME-GC-MS of authentic standards of the different 2-alkylfurans in the same amounts showed a clear increase in GC peak area with increasing length of the alkyl side chain, from 2-ethylfuran to 2-hexylfuran, following a sigmoid curve (Figure 2). For all α,β-unsaturated aldehydes tested, an increase in the 2-alkylfuran peak area was found with the addition of water and a $CuCl_2$ solution to the carbonyl compound and with the addition of phenylalanine to the model mixtures (Table 2). These results confirm the enhancing effect of the pro-oxidant copper ions on the 2-alkylfuran formation and thus suggest the involvement of oxidation processes in their formation from α,β-unsaturated aldehydes. The subsequent intramolecular cyclization of 4-hydroxy-2-alkenals

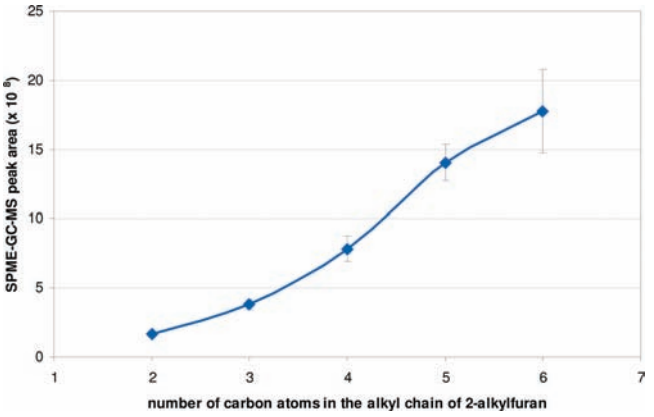
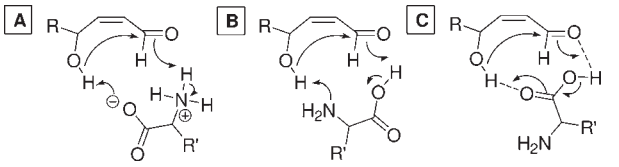


Figure 2. SPME-GC-MS peak area as a function of the length of the alkyl chain of a 2-alkylfuran (from 2-ethylfuran to 2-hexylfuran; 0.45 mg on 2 g of sand).

Scheme 2. Hypothesized Amino Acid Catalysis of the Cyclization of (*Z*)-4-Hydroxy-2-Alkenal by Three Possible Ways



into the corresponding 2-alkylfurans is believed to require high temperature,[15] but our results indicate that it can also be facilitated by amino acid catalysis. The resulting mechanism of 2-alkylfuran formation, involving the radical oxidation by means of oxygen, is proposed in Scheme 1. Because α-amino acids have received attention before as (enantioselective) catalysts of various transformations,[16] we hypothesize that amino acids can catalyze the cyclization of the (*Z*)-4-hydroxy-2-alkenals into the corresponding 2-alkylfurans, in several possible ways (Scheme 2). First, an amino acid can facilitate the cyclization process by acid/base catalysis (Scheme 2A). The zwitterionic form of the amino acid protonates the carbonyl group of the (*Z*)-4-hydroxy-2-alkenal, thus increasing its electrophilicity, while at the same time the hydroxyl function is deprotonated, increasing its nucleophilicity. An amino acid can regain its zwitterionic form when the amino group takes up a proton while the carboxyl group is deprotonated. This process as well may catalyze the cyclization of a (*Z*)-4-hydroxy-2-alkenal (Scheme 2B). Finally, the hydrogen-bonding ability of amino acids can be of high importance.[16] Thus, we present in Scheme 2C catalysis of the cyclization based on hydrogen bonding by the carboxyl group of the amino acid. The alcohol function of the side chain of serine, threonine, and tyrosine may also be relevant in this respect, as these amino acids showed the highest activity. Other relative differences between the amino acids tested will probably depend on their specific acid/base properties and on steric effects.

Because of their highly versatile nature and reactivity, amino acids may thus exert several functions in the myriad of reactions occurring during thermal treatment of food. Their condensation with carbohydrates in the Maillard reaction is of extreme importance in heated food products, but the catalysis of 2-alkylfuran formation described here illustrates their broad catalytic potential in food.

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