# Active pharmaceutical ingredients and amino acids as building blocks for new ionic liquids synthesis

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## Abstract

The synthesis of new ILs based on sodium docusate, an active pharmaceutical ingredient, and amino acids was presented.

## Introduction

The rapidly growing research interest in ionic liquids (ILs) is undoubtedly stimulated by the development of green chemistry. While a tremendous amount of recent research has focused on the physical properties of ILs, and more recently the chemical properties, the toxicity, a biological property, has been one of the most highly debated topics in this field.[1] Indeed, toxicity is also a tunable property of ILs, and given the similarities between many common IL building blocks and active pharmaceutical ingredients (APIs), one wonders the potential to utilize them as precursors, since they are low toxicity reagents.[2,3] Considering the green chemistry context, we found that amino acids and their derivatives have rarely been directly used to prepare the cations in ILs. Herein we report the synthesis of a series of new ionic liquids based on amino acids and sodium docusate, a pharmaceutical used as emollient.

## Results and Discussion

The formation of [AA]Doc is a simple metathesis reaction carried out by mixing an equivalent amount of esterified amino acid (glycine, alanine, phenylalanine, cysteine, triptophane) and sodium docusate, using acetonitrile as solvent (Figure 1). The mixture was stirred at room temperature during 16 h. The following step involved the solvent evaporation under vacuum, furnishing the desired products. The products were obtained in moderate to good yields (Table 1). All compounds were identified by NMR spectroscopy and/or melting point, when appropriate.

After the synthetic step, we have also tested the toxicity of the ILs. For this purpose, we chose the glycine derivative to do the oral and intraperitoneal acute evaluation in mice. The results indicated low toxicity (LD50 > 2000 mg/Kg) in according to the protocol 423 of the Organization for Economic Co-Operation and Development (OECD, 2001).

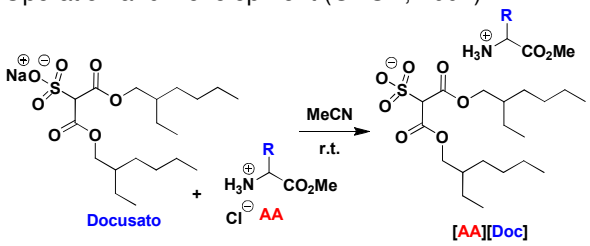


**Figure 1.** Synthetic route used to obtain the API-ILs.

**Table 1.** Amino acids used in this work and the product yields.

| Amino acid methyl esther | R | Yield (%) |
|---|---|---|
| Gly | H | 87 |
| Ala | $CH_3$ | 73 |
| Phe | $CH_2Ph$ | 60 |
| Cys | $CH_2SH$ | 45 |
| Tryp | $CH_2$-indol | 50 |

## Conclusions

The synthetic route applied in the present work was considered environmentally benefic and suitable to obtain a great variety of non-toxic API-ILs based on amino acids. In addition, this one-step procedure is an atom-economic reaction without any poisonous by-product.

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