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Synthesis of novel polyurethane polyesters using the enzyme *Candida antarctica* lipase B

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A novel enzymatic route has been used to synthesise standard and unusual polyester polyurethanes without employing the usual highly toxic isocyanate intermediates

The majority of reported enzymatic syntheses using lipases, are concerned either with the synthesis of optically active esters or alcohols, where the enantioselectivity of the enzyme steers the reaction product to a particular isomer,[1] or with the synthesis of polyesters.[2,3,4] Apart from the synthesis of sugar esters,[5] the hydrolysis[6] and transesterification[7] of sensitive esters (*e.g.* prostaglandin esters) and the work of Harffey *et al.* with epoxide esters,[8] the mild, low temperature aspects of enzymatic synthesis have not been exploited to full advantage as yet.

Polyester based polyurethanes have numerous applications in surface and textile coatings, adhesives and elastomers. These materials are manufactured from hydroxy terminated polyester resins made by high temperature Lewis acid catalysed condensation of a diacid and diol.[9] Subsequent reaction with highly toxic diisocyanates produce a polyurethane polymer.[10] The diisocyanates are derived from the even more toxic phosgene and the corresponding diamine.[11] Thus, the production of a narrow range of less toxic, low volatility (mainly aromatic) diisocyanates is limited to only a few companies in the world who are capable of operating the process safely.

There have been many attempts at non-phosgenation routes to diisocyanates and to the synthesis of polyurethanes without isocyanates. None of these has been successful commercially. In the conventional process the addition of the isocyanate must occur after esterification because the carbamate group begins decomposing at 160–180 °C,[12,13] well below the esterification temperature (typically 220 °C). However, the use of enzymatic methods allows us to reverse the conventional process by creating the urethane first and then using a low temperature enzymatic polyester synthesis to build the polymer. Thus, we were able to synthesise a novel series of biscarbamate esters and polyesters.

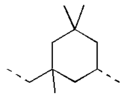
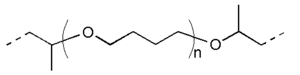
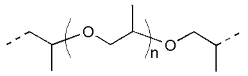
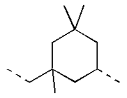
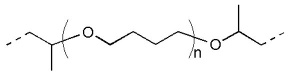
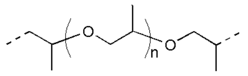
It was known from the work of Delaby *et al.*[14] in the 1950's that the carbamate group could be synthesised by the ring opening addition of a cyclic carbonate, such as ethylene carbonate **1a**, with a primary diamine. The product of this reaction being the bis(hydroxyethyl) carbamate (*e.g.* Scheme 1).

These diols have been used to form polymers by reacting the biscarbamates with methylol melamine to give cross-linked urethane containing polyether polymers.[15] These polymers had some of the properties of a polyurethane, but the need for high temperature stoving meant that some degradation took place.

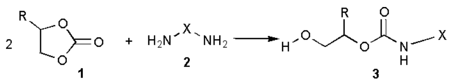
Enzyme catalysed esterification of bis(hydroxyethyl) carbamates derived from readily available diamines, affords a low temperature route to polyester polyurethanes avoiding the use of diisocyanates. This idea suggested two possible applications, firstly less hazardous syntheses of polymers (avoiding diisocyanates) that are analogues of existing polymers, secondly synthesis of novel polyester polyurethanes where the requisite diamine was available, but the diisocyanate was not, *e.g.* ethylenediamine is readily available, but ethylenediisocyanate is not as it is extremely toxic due to its volatility. Reactions with aliphatic diamines were performed as aliphatic diisocyanates are much more expensive and hazardous than aromatic ones.

Delaby *et al.* synthesised, bis(hydroxyethyl) hexamethylene carbamate **3a**, using ethylene carbonate **1a** and hexamethylenediamine **2a**.[16] Modifying their procedure slightly (omission of cooling), we produced compound **3a** (mp 94 °C) in 60% yield and high purity; by gel permeation chromatography (GPC) and ^{1}H NMR spectroscopy (Table 1).

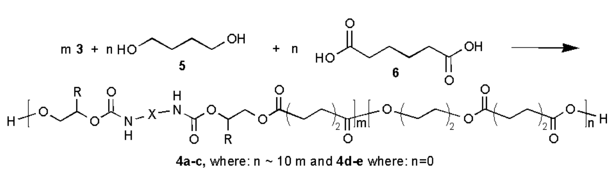
Table 1 Groups R and X present in the compounds **1**–**3** and polymers **4**

Compound	R	X
1a	H	—
1b	CH_3	—
2a	—	$-(CH_2)_6-$
2b	—	$-(CH_2)_2-$
2c	—	
2d	—	 *n* ~ 3
2e	—	 *n* ~1 or 2
3a, 4a	H	$-(CH_2)_6-$
3b, 4b	H	$-(CH_2)_2-$
3c, 4c	CH_3	
3d, 4d	H	 *n* ~ 3
3e, 4e	H	 *n* ~1 or 2

As the desired physical properties of the finished polyester polyurethane meant that the biscarbamate **3a** was unlikely to be used as the only diol component of the polyester, a co-polyester **4a** with butane-1,4-diol and adipic acid was synthesised using the biscarbamate as about 10% of the total diol (Scheme 2). The biscarbamate **3a** was dissolved in butane-1,4-diol **5** at 90 °C



Scheme 1 Synthesis of diurethane diols.



4a-c, where: n ~ 10 m and **4d-e** where: n=0

Scheme 2 Synthesis of a polyester polyurethane co-polymer.

under nitrogen, cooled to 60 °C and reacted with adipic acid **6** using Novozyme 435, a commercial preparation of supported *Candida antarctica* lipase B, as catalyst. The adipic acid **6** was added in portions so as not to inhibit the enzyme and the water formed was removed at about 100 mmHg over 2 days. GPC analysis using a 1000 Å column gave the molecular weight of the resulting polyester polyurethane **4a** as 9350 Daltons, compared to a polystyrene standard, with a dispersity of 1.75.

The polyester polyurethane **4a** is the analogue of a polybutane adipate polyester that has been partially chain extended with hexamethylene diisocyanate and which could be chain extended once more by the addition of further diisocyanate.

Next, the method was extended to the synthesis of urethane polyesters for which no equivalent isocyanate is available. Ethylenediamine **2b** was reacted with ethylene carbonate **1a** to give bis(hydroxyethyl) ethane carbamate **3b**, identical to a carbamate based on ethylene diisocyanate. The mp of the white crystalline compound was 93 °C. The yield was 60% after recrystallization; losses being due to the slight solubility of the product during a cold ethanol wash. Chromatography showed a single product free from starting materials. Once again, a butane-1,4-diol, adipic acid co-polyester **4b** was synthesised using the biscarbamate **3b** as 10% of the diol component. The molecular weight was found to be 4500 Daltons by GPC, with a dispersity of 2.4. This novel polyester was found to be extremely water soluble, due to the preponderance of ethane groups in the polymer. Such a water soluble polymer may well have applications in water soluble polyurethane coatings or adhesives.

One major problem associated with the commercialisation of a new process using novel intermediates is the need for costly toxicological testing of the compounds. The EINECS regulations are relaxed if the novel compound does not leave the reactor and if the final product is a high molecular weight polymer. Thus, as butane-1,4-diol **5** does not react with either of the reactants, the toluene solvent can be replaced with butane-1,4-diol **5**. IR spectroscopy and GPC analysis confirmed completion of the reaction with diamine **2b**; the product **3b** being a clear solution at 60 °C and a white waxy solid on cooling. Novozyme 435 and the requisite amount of adipic acid **6** were added to the reaction product **3b** to give a polyester **4b** with a molecular weight of about 1500 Daltons. GPC gave the molecular weight as 2200 M_n, 4640 M_w with a dispersity of 2.1. The acid number was 0.7 mg KOH g^{-1} and the hydroxyl number 78 mg KOH g^{-1}; this end group analysis gave a molecular weight of 1488 Daltons. There is no reason why this principle of using a diol from the second stage esterification as the diluent in the formation of the biscarbamate cannot be extended to the synthesis of any biscarbamate.

As it provides a useful polymer substituent, isophorone diamine **2c** was reacted with propylene carbonate **1b** to give the biscarbamate **3c**. GPC analysis showed that the reaction had gone to completion with no reactants remaining. This biscarbamate **3c** was converted to a co-polyester polyurethane **4c** in the usual manner. GPC gave the molecular weight, M_w, as 6000 and the dispersity as 2.14. The acid number was 2.0 mg KOH g^{-1}.

α,ω-Polytetramethylene ether diols are used extensively in the manufacture of high performance polyurethane elastomers and coatings. There are no equivalent diisocyanates available, but the related diamine **2d** is available by the reaction of an α,ω-polytetramethylene ether diol with acrylonitrile followed by hydrogenation to give the bis(1-aminoprop-2-yl)polytetramethylene ether **2d** of molecular weight 350. The biscarbamate **3d** of diamine **2d** was synthesised by reaction with ethylene carbonate **1a**.

The product **3d** was a reddish viscous liquid. NMR analysis showed that all the ethylene carbonate **1a** had reacted, however there was a trace of unreacted amine remaining. Because of the substantial polyether backbone of the diamine **2d** it was not thought necessary to add any butane-1,4-diol **5** to the biscarbamate **3d** in order to form a useful polyester polyurethane. Therefore, adipic acid **6** and Novozyme 435 were added and after heating at 60 °C under reduced pressure for 48 hours the final polymer **4d** had a molecular weight of 6500 by GPC and an acid number of 5.0 mg KOH g^{-1}. The combination of the ester groups and the ether backbone gave a polymer that was not soluble in any of the common solvents. It was thought that this material would make an excellent intermediate in the manufacture of solvent resistant coatings.

The above reaction was extended to the related polyoxypropyleneamine **2e**, Jeffamine D230. The amine was added to the ethylene carbonate **1a** as before, however, the exotherm was substantially less than with any of the previous amines and thus the reaction was maintained at 80°C overnight. TLC and ^{1}H NMR spectroscopy indicated that the reaction had gone to completion with only a trace of residual amine remaining. This biscarbamate **3e** was also converted to polyester in the same manner as the others and as for polymer **4d**, the finished polyester **4e** was a brown viscous liquid the molecular weight was 6500 Daltons by GPC and the acid number was 2 mg KOH g^{-1}.

We would like to thank Baxenden Chemicals Ltd., Accrington, UK, who have filed a patent on these reactions and the resulting compounds, for their support.

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