[18] N. Berova, K. Nakanishi in *Circular Dichroism: Principles and Applications* (Eds.: N. Berova, K. Nakanishi, R. W. Woody), Wiley-VCH, New York, **2000**, pp. 337–382.

[19] We found that thin films of these materials do not aggregate even with extended thermal annealing at 160 °C. Possibly the PPE main chains are collinear and kept apart by the presence of the pentiptycene groups.

[20] The saturation vapor pressure of TNT at 22 °C is 8.02×10^{-6} mmHg or about 10 ppb. *Handbook of Physical Properties of Organic Chemicals* (Eds.: P. H. Howard, W. M. Meylan), CRC, Boca Raton, FL, **1997**.

[21] For comparison, other electronic polymers reportedly decreased their fluorescence intensity by 8.2 % after exposure to similar vapor concentrations with turbulent flow for 10 min (H. Sohn, R. M. Calhoun, M. J. Sailor, W. C. Trogler, *Angew. Chem. Int. Ed.* **2001**, *113*, 2162; *Angew. Chem. Int. Ed.* **2001**, *40*, 2104). Hence **3**, which was studied under static conditions, is at least 560 times more sensitive.

[22] Y. Liu, R. C. Mills, J. M. Boncella, K. S. Schanze, *Langmuir* **2001**, *17*, 7452; G. A. Bakken, G. W. Kauffman, P. C. Jurs, K. J. Albert, S. S. Stitzel, *Sens. Actuators B* **2001**, *79*, 1.

[23] Y.-S. Yang, T. M. Swager, *J. Am. Chem. Soc.* **1998**, *120*, 11864.

[24] The CD and absorption spectra end at 50:50 chloroform:methanol as the rigid, gridlike aggregates precipitate readily at higher methanol content. The fluorescence spectra could be recorded up to 30:70 chloroform:methanol as the concentration of the polymer was only 1/10 of that of the absorption studies and therefore precipitation occurred at higher methanol concentrations.

[25] Similarly, **3** had a photoluminescence efficiency which was four times higher than that of **2** in films of identical optical density.

High-Throughput Multilevel Performance Screening of Advanced Materials

Radislav A. Potyrailo* and James E. Pickett

High-throughput screening and combinatorial chemistry have been successfully extended from pharmaceutical applications into other scientific disciplines.[1] Performance of rapidly fabricated compounds is typically evaluated by relating results of high-throughput analysis to the intrinsic properties of starting materials or final products.[2] We report a general scheme for screening of complex materials developed by using high-throughput and combinatorial methods, where simple screening for intrinsic properties of starting materials or final compounds does not provide information about long-term material performance.

Our general approach employs fabrication of materials arrays followed by their testing against single or several performance parameters at *multiple* levels. This testing process imitates the end-use application and alters materials properties in a detectable manner that is impossible to quantitatively predict using existing knowledge.[3] Our scheme of high-throughput evaluation of advanced materials fabricated by using high-throughput and combinatorial methods is very general and includes diverse testing methodologies such as solar radiation, mechanical stress, aggressive fluids, heat, and others. Tested arrays are further analyzed by using high-throughput screening (HTS) tools.

We demonstrated our strategy for high-throughput performance screening of polymeric materials. Weathering is a critical consideration in the development of new engineering thermoplastics for outdoor applications.[4] A determining factor in the outdoor weathering lifetime of these materials is the received UV radiation dose. It leads to material photodegradation that initially causes the loss of appearance such as surface discoloration and gloss loss.[5,6] Other environmental (humidity, temperature, frequency of light/dark cycles) and material (catalyst residues, crystallinity, molecular weight, end groups) factors do not appreciably affect the appearance of engineering thermoplastics upon weathering.[4,7] These factors, however, do have a pronounced effect on other types of polymers.[4,6] Additives and pigments (typical loadings of 0.01–5 wt %) greatly affect the stability of engineering and other types of polymers.[8] Thus, studies of polymer–additive and polymer–pigment combinations are of great importance.

Resistance toward weathering presents a particular challenge for HTS since exposure times for adequate outdoor weatherability testing are thousands of hours.[4] In principle, acceleration of this process can be achieved either by increasing the level of environmental stress or by very early detection of material degradation. In laboratory weathering methods, a dose equivalent to one year of exposure to conditions in Florida can be reduced to about 1100 h.[9] However, a further acceleration of materials weathering to the HTS level becomes problematic because of loss of correlation with traditional test methods.[4,8,10]

We use fluorescence imaging and spectroscopy to quantify photodegradation in arrays of materials at short exposure times that open up HTS capabilities in weathering studies. Our libraries combine the variables of polymer composition, pigment type, and exposure time, but are easily extendable to incorporation of stabilizers and other additives at different loadings that may affect the rate of degradation.

Unlike traditional measurements of weatherability-related appearance based on color changes and gloss loss,[4,8b,11] fluorescence analysis[12] advances the studies of polymeric materials libraries produced by using high-throughput methods to a previously unavailable level of capabilities. Fluorescence detects trace amounts of weathering degradation products and thus requires a considerably shorter testing time. Measurements are performed on both lightly and highly colored samples with a comparable level of sensitivity. Because fluorescence light is isotropic, the whole combinatorial library is imaged without the need for an integrating sphere or a goniophotometer. Different fluorescence excitation–emission conditions can be selected to analyze different fluorescent species.

To demonstrate the applicability of our screening strategy, three types of aromatic polymers (polycarbonate, PC; poly(butylene terephthalate), PBT; and their 45/55 wt % blend, PC/PBT) were made in combination with two types of pigments (rutile TiO_2 and carbon black, CB) and tested under

---

[*] Dr. R. A. Potyrailo, Dr. J. E. Pickett
General Electric Company
Global Research Center
Niskayuna, NY 12309 (USA)
Fax: (+1) 518-387-5604
E-mail: Potyrailo@crd.ge.com

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

11 levels of weathering conditions. The pigments were selected to provide a wide range of potential weathering performance of materials. The mass loadings (2 and 0.6 wt% for TiO_2 and CB, respectively) were within the application range in polymers.[8] The testing scheme of these arrays of polymer compositions is shown in Figure 1a. For comparison of fluorescence with conventional methods, the maximum exposure dose (1030 kJ m^{-2} at 340 nm) was accumulated over 417 h.

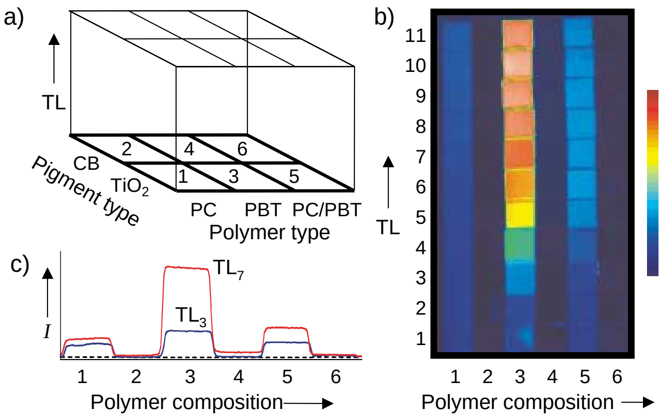


Figure 1. Screening of complex materials developed by using high-throughput methods under multilevel performance test conditions. a) Testing scheme for the arrays of polymeric materials with pigment compositions and multiple test levels (TL_x). b) Fluorescence image of 11 arrays of polymeric materials after weatherability testing at 11 levels. c) Cross sections of arrays 3 (TL_3) and 7 (TL_7) demonstrating fluorescence signals in different polymeric compositions. Dotted line, background.

We determined the amount of UV-induced degradation in the arrays of polymeric materials using fluorescence imaging and spectroscopy. A fluorescence image of 11 arrays is shown in Figure 1b. These experiments demonstrated that fluorescence intensity increases as a function of exposure dose and depends on both the nature of the polymer and the nature of the pigment. Fluorescence imaging revealed the increase in fluorescence intensity of all dark polymer samples pigmented with CB indicating polymer degradation (see Figure 1c, polymer compositions 2, 4, and 6), although the emission was about 20× weaker than that for the same polymers pigmented with TiO_2.

For detailed analysis of weatherable performance of arrays, we coupled a fiber-optic spectrograph to automatically operate with a X–Y translation stage. Results of these experiments are presented in Figure 2. Using multilevel performance screening, we found similar kinetic rates of weathering of polymers with quite different pigments. In contrast, traditional analysis of weathering of dark polymers involves measurements of gloss loss after the surface is heavily degraded (accumulation of 800–1000 kJ m^{-2} dose) and does not provide kinetic information at early weathering stages.

Comparison of fluorescence and color analysis of TiO_2-pigmented polymers is presented in Figure 3.[13] Color is analyzed as an increase in yellowness index (YI)[4,8b,11] which corresponds well to how the human eye perceives yellowness of lightly colored materials. In color analysis, YI is a well-established value of merit.[4,8b,11,14] However, as shown in the inset of Figure 3, fluorescence is much more sensitive than YI

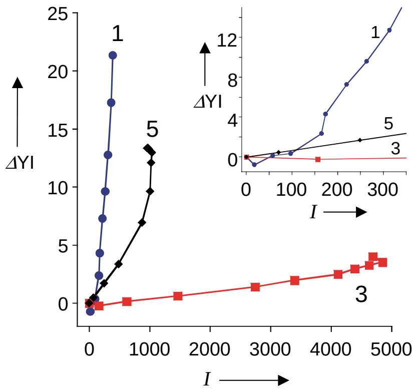


Figure 3. Correlation between fluorescence and color analysis of TiO_2-pigmented polymers 1–6 (see Figure 1a). Inset, early stage of weatherability studies. $\Delta YI = YI - YI_o$, where YI_o is at test level TL_1.

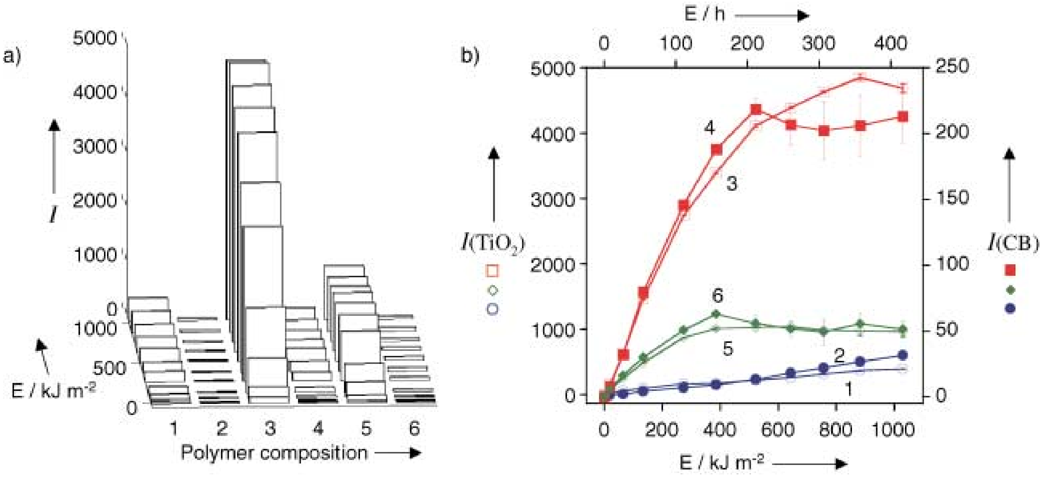


Figure 2. a) Effect of increasing exposure dose on the weatherability of arrays of polymer compositions 1–6 (see Figure 1a). b) High-throughput determination of weatherability kinetics of arrays of polymer compositions 1–6. Open markers, TiO_2 pigment; filled markers, CB pigment.

at early stages of polymer degradation. Also, the problems of bleaching and instability of colorants at early stages of weathering tests do not confound it.[15] The fluorescence intensity alone slightly decreases at prolonged exposures as shown in Figure 3 for PBT and PC/PBT. In addition to fluorescence intensity determinations, distortions and shifts of excitation and emission peaks can also serve as a polymer-lifetime prediction tool.[16]

We evaluated the capabilities of our method by determining the smallest exposure time required to detect a change in fluorescence signal.[17] For the TiO_2-pigmented polymers, the fluorescence signal change can be detectable after only 28, 19, and 26 min of irradiation for PC, PBT, and PC/PBT, respectively. Similarly, this time was 138, 30, and 72 min for the CB-pigmented PC, PBT, and PC/PBT, respectively. Using fluorescence, the throughput of screening can be increased by 200–650-fold and 150–800-fold, compared to determination of color change and gloss loss, respectively. Thus, information about the kinetics of photodegradation is available much sooner.

The multilevel screening provides robust ranking of material performance. Figure 4 shows the ranking of weatherability of polymeric materials with 18.9 and 522 kJ m^{-2} exposures for each polymer type. The ranking of the weatherability at the smallest used exposure is the same as at more advanced exposure levels when the analytical signal is 10–25 times stronger.[18] Similar to evaluation of discoloration, this method shows utility for formulation/stability development within a preselected material type, however with much higher screening throughput.[19]

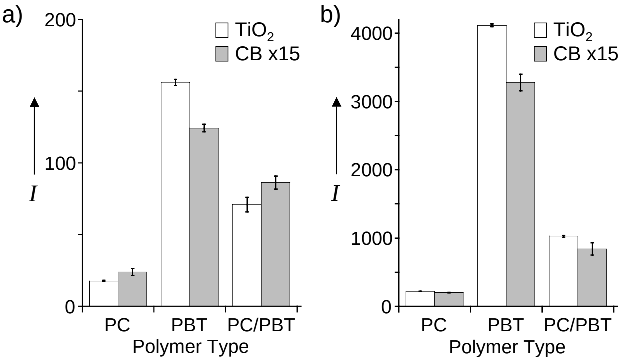


Figure 4. Applicability of fluorescence analysis for ranking of materials weatherability at a) 18.9 kJ m^{-2} and b) 522 kJ m^{-2} stages of performance testing.

In summary, we present a new approach for high-throughput screening of complex material systems when performance of materials cannot be evaluated based on simple measurements of their intrinsic properties immediately after fabrication. Multiple levels of end-use testing conditions provide more reliable ranking of performance of materials made by using high-throughput and combinatorial methods and serve as a robust predictive tool. With a combination of testing and high-sensitivity analysis steps in a single discovery cycle, it should be possible to design screening systems for just about any advanced material.

Experimental Section

Polymer/pigment combinations were injection molded by using small-scale equipment. Individual $2 \times 12.5 \times 12.5$ mm elements of all six polymer compositions were arranged in a holder in 11 replicate rows as a 6×11 array. Multilevel performance testing of polymeric arrays was done in a borosilicate-filtered Xe-arc Weatherometer (Atlas Ci4000, 0.75 W m^{-2} irradiance at 340 nm). The exposure dose ranged from 18.9 to 1030 kJ m^{-2} (at 340 nm) and was produced by unmasking certain arrays of six polymer compositions at predetermined time points.

Fluorescence imaging was done with a cooled CCD camera (Roper Scientific) through a 420 nm cutoff long-pass filter. Excitation was provided by a 450-W Xe arc lamp and a 340 nm interference filter. Fluorescence spectroscopic measurements were performed by using a custom-built automatic modular system (Xe arc lamp, monochromator, bifurcated fiber-optic reflection probe, spectrograph, X–Y translation stage). Reference measurements of color and gloss were performed on MacBeth 7000 and BYK-Gardner Micro Trigloss instruments, respectively. Minimal exposures for color and gloss measurements were 250–500 kJ m^{-2} (100–200 h) and 800–1000 kJ m^{-2} (320–400 h), respectively.

Received: April 29, 2002
Revised: September 3, 2002 [Z19189]

---

[1] a) B. Jandeleit, D. J. Schaefer, T. S. Powers, H. W. Turner, W. H. Weinberg, *Angew. Chem.* **1999**, *111*, 2648; *Angew. Chem. Int. Ed.* **1999**, *38*, 2494; b) "Combinatorial Approaches to Materials Development": *ACS Symp. Ser.* **2002**, *814*; c) "Combinatorial and Arficial Intelligence Methods in Materials Science": *MRS Symp. Proc.* **2002**, *700*.

[2] Examples of measured properties of reaction components and final products in combinatorial libraries: a) catalytic properties, A. Holzwarth, H.-W. Schmidt, W. Maier, *Angew. Chem.* **1998**, *110*, 2788; *Angew. Chem. Int. Ed.* **1998**, *37*, 2644; H. Su, E. S. Yeung, *J. Am. Chem. Soc.* **2000**, *122*, 7422; b) polymer molecular weight, S. Brocchini, K. James, V. Tangpasuthadol, J. Kohn, *J. Am. Chem. Soc.* **1997**, *119*, 4553; c) thin-film dewetting, J. C. Meredith, A. P. Smith, A. Karim, E. J. Amis, *Macromolecules* **2000**, *33*, 9747; d) materials resistivity, X.-D. Xiang, X. Sun, G. Briceño, Y. Lou, K.-A. Wang, H. Chang, W. G. Wallace-Freedman, S.-W. Chen, P. G. Schultz, *Science* **1995**, *268*, 1738; e) mechanical properties, J.-C. Zhao, *Adv. Eng. Mater.* **2001**, *3*, 143.

[3] Examples of high-throughput performance testing: a) R. A. Potyrailo, D. R. Olson, B. J. Chisholm, M. J. Brennan, J. P. Lemmon, J. N. Cawse, W. P. Flanagan, R. E. Shaffer, T. K. Leib, Pittcon 2001 (New Orleans, LA), **2001**, paper 992; b) C. Meredith, J.-L. Sormana, A. Tona, H. Elgendy, A. Karim, E. Amis, *Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem.* **2001**, *42*, 649 – 650; c) J. W. Gilman, COMBI 2002 (San Diego, CA), **2002**.

[4] G. Wypych, *Handbook of Material Weathering*, ChemTec, Toronto, **1995**.

[5] J. E. Pickett, K. K. Webb, *Makromol.Chem.* **1997**, *252*, 217.

[6] Loss of appearance in engineering thermoplastic materials is observed much earlier than changes in physical, solution, and mechanical properties. See: A. Davis, D. Sims, *Weathering of Polymers*, Elsevier, London, **1986**.

[7] J. E. Pickett, *Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem.* **2001**, *42*, 424.

[8] a) *Plastics and Coatings. Durability, Stabilization, Testing* (Ed.: R. A. Ryntz), Hanser, Cincinnati, **2001**; b) H. Zweifel, *Plastics Additives Handbook*, Hanser, Munich, **2001**.

[9] J. E. Pickett, J. E. Moore, *Makromol.Chem.* **1995**, *232*, 229.

[10] V. D. Sherbondy in *Paint and Coating Testing Manual* (Ed.: J. V. Koleske), ASTM, Philadelphia, **1995**, chap. 53.

[11] V. Shah, *Handbook of Plastics Testing Technology*, Wiley, New York, **1998**.

[12] H. Shah, I. B. Rufus, C. E. Hoyle, *Macromolecules* **1994**, *27*, 553.

[13] For exposure time and dose, see the Supporting Information.

[14] Mechanisms of color formation in engineering aromatic thermoplastics upon weathering are complex and still are poorly understood. Suggested mechanisms include oxidation of aromatic rings of polymers, side chain oxidation, and others. See: A. Factor in *Polymer*

Durability. Degradation, Stabilization, and Lifetime Prediction (Eds.: R. L. Clough, N. C. Billingham, K. T. Gillen), ACS, Washington, DC, **1996**, pp. 59–76 (*Adv. Chem. 249*).

[15] N. D. Searle, N. L. Maecker, L. F. E. Crewdson, *J. Polym. Sci. A* **1989**, *27*, 1341.

[16] Excitation and emission spectra of TiO_2- and CB-PBT showed only an exposure-dependent intensity increase, while TiO_2- and CB-PC and PC-PBT showed also distortions and shifts of excitation and emission spectral bands. This suggested that upon weathering the number of different types of generated fluorescent chromophores was roughly constant in PBT and was increasing in PC. For fluorescence spectra, see the Supporting Information.

[17] Calculated for the signal-to-noise ratio of three, see: J. D. Ingle, Jr., S. R. Crouch, *Spectrochemical Analysis*, Prentice Hall, Englewood Cliffs, NJ, **1988**.

[18] For additional experiments exploring further improvement of the screening throughput, see the Supporting Information.

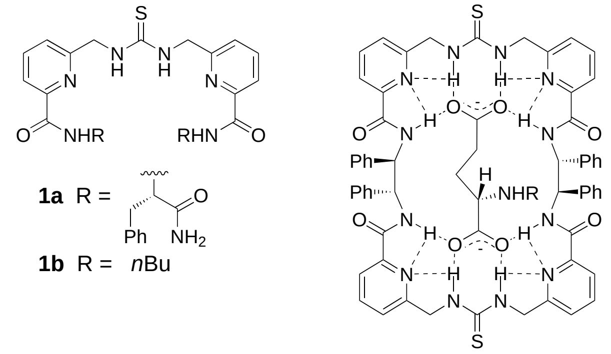
[19] Measurements of polymer fluorescence can be applicable for a variety of aromatic and other types of polymers during weathering testing. If fluorescent additives or initial impurities in polymers present a problem, molecular probes for analysis of surface oxidation products may be more applicable. See: S. R. Holmes-Farley, G. M. Whitesides, *Langmuir* **1986**, *2*, 266; V. B. Ivanov, J. Behnisch, A. Hollaender, F. Mehdorn, H. Zimmermann, *Surf. Interface Anal.* **1996**, *24*, 257.

A Highly Enantioselective Receptor for *N*-Protected Glutamate and Anomalous Solvent-Dependent Binding Properties**

Sara Rossi, Graham M. Kyne, David L. Turner, Neil J. Wells, and Jeremy D. Kilburn*

The development of enantioselective receptors continues to be a challenging endeavor for supramolecular chemists, and enantioselective recognition of biologically relevant molecules in competitive solvents is particularly demanding.[1] Although numerous receptors have been developed for dicarboxylic acids and dicarboxylates,[2] only a few enantioselective receptors for chiral dicarboxylic acids (in the neutral diprotonated form) have been described,[3] and very few examples of enantioselective receptors for chiral dicarboxylates have been reported.[4]

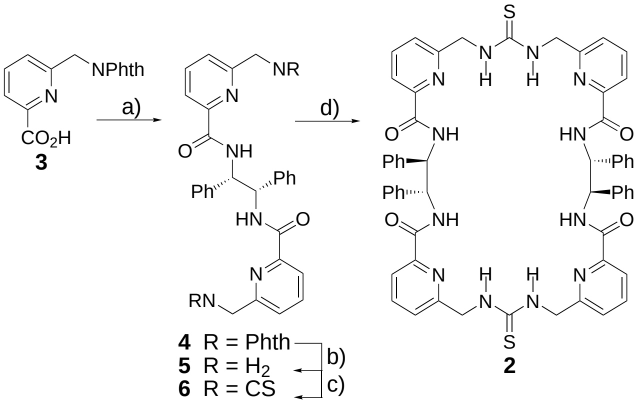
We recently described an acyclic monothiourea receptor **1a**, which bound a range of *N*-protected amino acid carboxylate salts with modest enantioselectivity.[5] Building on this work, we have now prepared macrocyclic receptor **2**, which features two thiourea moieties flanked by carboxypyridines and separated by a chiral diamine. The receptor was designed to produce a chiral pocket for dicarboxylates by forming up to eight hydrogen-bonding interactions with the carboxylate oxygen atoms and intramolecular hydrogen bonding with the pyridine unit to help preorganize[6] the receptor (Scheme 1). Binding measurements, by NMR titration and isothermal calorimetry, indicate that the macrocycle exhibits strong and highly enantioselective 1:1 binding of *N*-Boc-L-glutamate (as the dicarboxylate dianion) in relatively polar solvents (CH_3CN, DMSO) and that complexation involves a large, favorable entropic contribution. Remarkably, however, no binding of *N*-Boc-glutamate by the macrocycle is observed in a less polar solvent ($CDCl_3$).



Scheme 1. Acyclic monothiourea **1** and the proposed complex of *N*-Boc-L-glutamate with macrocycle **2**. Boc = *tert*-butoxycarbonyl.

The synthesis of receptor **2** was readily achieved by coupling acid **3**[5] with (*S*,*S*)-1,2-diphenylethylenediamine to give bisphthalimide **4** (Scheme 2). Removal of the phthalimide protecting groups and treatment of the resulting bisamine **5** with CS_2 and DCC produced the bis(isothiocyanate) **6**. A further equivalent of bisamine **5** was added to bisisothiocyanate **6**, in the presence of DMAP, by syringe pump over three hours to yield the macrocyclic bisthiourea **2** in 26% yield.

The ^1H NMR spectrum[7] of macrocycle **2** in $CDCl_3$ at room temperature is poorly resolved, with very broad signals for all protons, and resolution is not improved at higher temper-



Scheme 2. Reagents: a) $SOCl_2$; (1*S*,2*S*)-(−)-1,2-diphenylethylenediamine, DMAP, CH_2Cl_2 (68%); b) $N_2H_4 \cdot H_2O$, EtOH (84%); c) CS_2, DCC, CH_2Cl_2; d) simultaneous addition of 1 equiv of **5** and 1 equiv of **6** by syringe pumps over 3 h (26% over steps c and d). DMAP = 4-dimethylaminopyridine, DCC = *N*,*N*′-dicyclohexylcarbodiimide.

---

[*] Prof. J. D. Kilburn, S. Rossi, G. M. Kyne, Dr. D. L. Turner, N. J. Wells
Department of Chemistry
University of Southampton
Southampton, SO17 1BJ (UK)
Fax: (+44) 2380-596-805
E-mail: jdk1@soton.ac.uk

[**] We thank the Commission of the European Union (TMR Network grant "Enantioselective Separations" ERB FMRX-CT-98-0233) for financial support and postgraduate fellowships (S.R.) and the EPSRC for a quota studentship (G.M.K.).

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.