80 μmol) in dry CH_2Cl_2 (1 mL) was degassed, and a 2 M solution of Me_3Al (80 μL, 0.16 mmol in toluene/heptane, Aldrich) was added at room temperature under argon and the mixture was then stirred for 60 min. Immediately after evolution of gas had stopped the solution obtained (containing **5**) was cooled to 0 °C, equal amounts of benzaldehyde (0.16 mL, 1.6 mmol) and diacetone alcohol (0.20 mL, 1.6 mmol) were added simultaneously to the solution. After evolution of gas ceased the clear light yellow solution obtained was allowed to warm up to room temperature. The mixture was stirred for 43 h then poured into a 0.5 M HCl solution (5 mL) and extracted with diethyl ether. The combined extracts were dried over $MgSO_4$. Evaporation of solvents and purification of the residual oil by flash chromatography (silica gel, hexane/ethyl acetate, 1/5) gave 3-oxo-1-phenyl-butan-1-ol (**10a**, 164 mg, 1.0 mmol) as a colorless oil (62 % yield). ^{1}H NMR (200 MHz, $CDCl_3$, 20 °C, $CHCl_3$ ref.$\delta = 7.27$): $\delta =$ 7.4 – 7.2 (m, 5H, Ph), 5.1 (m $J = 3.3$ Hz, $J' = 3.7$ Hz, $J'' = 8.1$ Hz, 1H; CH), 3.3 (d, $J = 3.3$ Hz, 1H; OH), 2.83 (dd, $J = 8.1$ Hz, $J' = 17.6$ Hz, 1H; CH_2), 2.79 (dd, $J = 3.7$ Hz, $J' = 17.6$ Hz, 1H; CH_2), 2.1 (s, 3H; CH_3).

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[10] Aluminum complexes used as catalysts: a) complex **3** was generated by treatment of binaphthol with one equivalent of Me_3Al (in toluene/heptane, Aldrich); b) complexes **4a**, **4b**, and **5** were generated by the treatment of the corresponding biphenols of binaphthol with two equivalents of Me_3Al; c) complex **6** was generated by treatment of biphenol with two equivalents of Et_2AlCl (in hexane, Aldrich); d) isopropoxide **7** was from Fluka and was used as supplied; e) alkoxide **8** was formed in situ by treatment of Me_3Al by 20 equivalents of diacetone alcohol; f) for use as a reagent the alkoxide **8** was formed by treatment of Me_3Al with three equivalents of diacetone alcohol.
[11] The reaction of **9b** (entry 5, Table 1) produced benzophenone as a side product, which was detected while monitoring the reaction by thin-layer chromatography.
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Applications of a Nonlinear Organic Reaction of Carbamates To Proliferate Aliphatic Amines

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We recently proposed the concept of acid proliferations in which acid-sensitive compounds (referred to as acid amplifiers) generate strong acids in a nonlinear manner.[1] The compounds developed so far undergo fragmentations to form sulfonic acids which are acidic enough to lead to autocatalytic decomposition. The addition of the acid amplifiers to chemically amplified photoresists (composed of photoacid generators and acid-sensitive polymers[2]) enhances the photosensitivity and improves resist performance.[3] This happens because the number of photogenerated acid molecules increases markedly as a result of the acid proliferation of the doped acid amplifiers. On the other hand, despite the widespread use of base catalysis in organic chemistry, analogous chemically amplified resist systems relying on the photochemical liberation of a basic species[4] has received far less attention. This may be because of relatively low quantum yields for photobase photogeneration, which leads to low photosensitivity. If base molecules could be produced, for example, by the base-catalyzed transformation of a precursor, to increase the amount of basic species in a geometric progression, the rates of subsequent base-catalyzed reactions should be enhanced considerably, in a manner similar to that of systems involving acid proliferation. This idea led us to the molecular design and synthesis of base precursors which can be termed "base amplifiers"; this name is appropriate because the compounds generate more base molecules than they react with. Base proliferation processes can be coupled with versatile base-catalyzed reactions to develop various types of nonlinear chemical transformation. We were particularly interested in combinating a base amplifier with a photobase generator because a tiny amount of a photogenerated base may enhance rates of subsequent base-catalyzed reactions owing to the autocatalytic decomposition of the base amplifier. This process leads to the improvement of photosensitivity of base-sensitive photopolymer systems. Herein we describe novel base-sensitive compounds as base amplifiers that improve the efficiency of the photoinduced insolubilization of poly(glycidyl methacrylate) (PGMA) as a base-sensitive polymer.[5]

Our efforts have focused on the development of base amplifiers which should fulfill the following requirements: first, a base amplifier should undergo a base-catalyzed decomposition to liberate a base, thus leading to autocatalytic decomposition; second, a base amplifier should be thermally stable in the absence of a base under reaction conditions that advance both the autocatalytic decomposition and the subsequent base-catalyzed reaction; third, the liberated base

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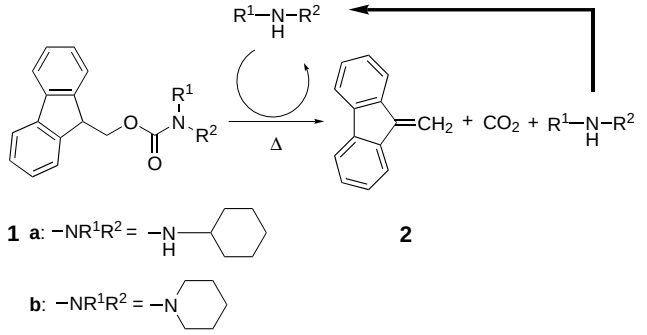
should be strong enough to catalyze subsequent chemical reactions and thus cause a nonlinear chemical transformation. Consequently, we designed 1-(9-fluorenylmethoxycarbonyl)-cyclohexylamine (**1a**) and 1-(9-fluorenylmethoxycarbonyl)piperidine (**1b**) as base amplifiers, taking note that the 9-fluorenylmethoxycarbonyl group is a useful protective groups for amino groups in peptide synthesis.[6] Although the carbamate compound **1a** was reported[6] as a demonstration of the utility of the 9-fluorenylmethoxycarbonyl group in peptide synthesis, information on the decomposition kinetics of **1a** with reference to the potential to proliferate amines has not been described. The carbamate compounds **1a** and **1b** were isolated as thermally stable crystals from the reaction of 9-fluorenylmethyl chloroformate with cyclohexylamine and piperidine, respectively. The base-catalyzed decomposition of **1a** and **1b** probably represents an E1cB-elimination to release the corresponding amines, cyclohexylamine and piperidine, respectively, which are sufficiently basic to lead to the decomposition of parent molecules (Scheme 1).[6]



Scheme 1. Autocatalytic fragmentation of **1**.

The thermal behavior of **1a** in 1,4-[D_8]dioxane at 100 °C was monitored by ^{1}H NMR spectroscopy. Figure 1 shows both the consumption of **1a** and the formation of dibenzofulvene (**2**) in the presence and absence of a catalytic amount of cyclohexylamine. The carbamate **1a** disappeared immediately, with a sigmoidal time conversion curve, in the presence of cyclohexylamine to form **2.** This reaction is quantitative (complete decomposition of **1a**) which indicates that the fragmentation of **1a** is autocatalytic leading to the proliferation of amines (Scheme 1). On the other hand, the carbamate **1a** was thermally stable in the absence of cyclohexylamine under the conditions that advance the autocatalytic decomposition reaction. The carbamate **1b** also showed the autocatalytic behavior in 1,4-[D_8]dioxane at 100 °C in a similar manner to **1a** except that the decomposition rate of **1b** is faster than that of **1a**. The difference in decomposition rates results from the basicity of the amines proliferated from the base amplifiers, **1a** and **1b**; the pK_a values of the conjugated acids of cyclohexylamine and piperidine are 10.64[7] and 11.22,[7] respectively.

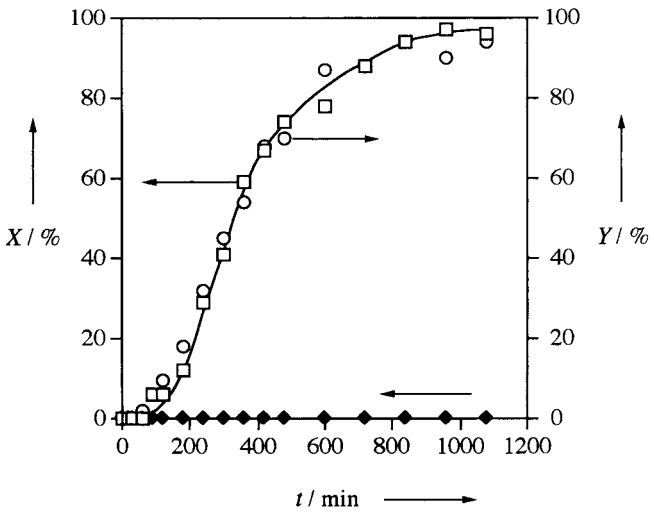
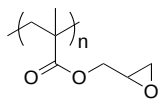
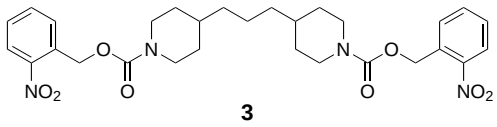


Figure 1. The consumption (X) of **1a** (70 mmol dm^{-3})(□) and the formation (Y) of dibenzofulvene (**2**) (○) as a function of heating time (t) in the presence of cyclohexylamine (11 mmol dm^{-3}), as well as the conversion of **1a** in the absence of cyclohexylamine (◆) in 1,4-[D_8]dioxane at 100 °C.

PGMA becomes insoluble in the presence of a photobase generator upon UV irradiation and after post-exposure baking, owing to the crosslinking reaction of epoxy groups with a photogenerated amine, which functions as a negative-tone photoresist.[8] Therefore, to examine the enhancement effect of **1a** and **1b** on the photoinsolubilization of the



PGMA



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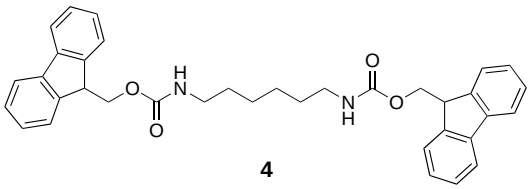

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polymer, a thin film of PGMA, doped with either the carbamate compound **1a** or **1b**, and 1,3-bis[(2-nitrobenzyl)-oxycarbonyl-4-piperidyl]propane (**3**)[4c] as a photobase generator was exposed to UV light, followed by heating. However, no enhancement of the photoinsolubilization was observed in the presence of **1a** or **1b**, probably because of the volatility of cyclohexylamine and piperidine generated from the base amplifiers during the post-exposure baking. These facts led us to generate 1,6-diaminohexane (**5**) that has a higher molecular weight which should reduce its volatility; compound **5** was generated from bis[(9-fluorenylmethoxy)-carbonyl]hexane-1,6-diamine (**4**). In addition, the liberated **5** was expected to be an efficient crosslinker of epoxy polymers because of the double reactivity of each terminal primary

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amino group towards epoxy residues. A spin-cast film of PGMA doped with **3** and **4** was exposed to UV light, then heated at 110 °C for 15 min. This was followed by solvent development to obtain photosensitivity curves. As shown in Figure 2 the exposure time required for the insolubilization is considerably reduced in the presence of **4**. The sensitivity,

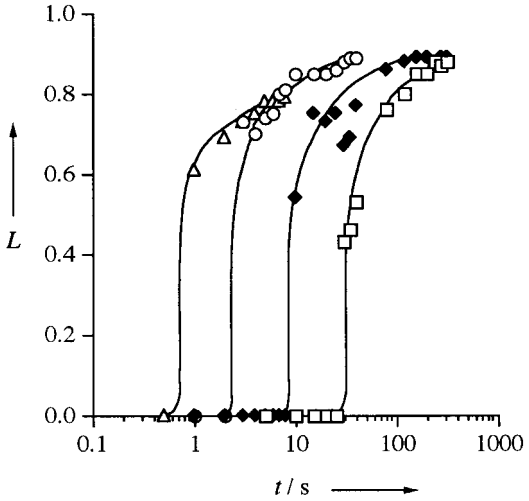

Figure 2. Photosensitivity curves of PGMA films containing 10 wt % of the photobase generator **3** in the absence of (□) and in the presence of 2 wt % (◆), 4 wt % (○), and 9 wt % of **4** (△), respectively. *L* and *t* denote normalized film thickness and irradiation time, respectively.

which is defined here as the irradiation time required for the reduction of normalized film thickness by half, is much improved by factors of 4, 20, and 50 by the addition of 2, 4, and 9 wt % of **4**, respectively. These results indicate that the photosensitivity enhancement arises from the proliferation reaction of **4** that generates the diamine **5** in a nonlinear manner, which by crosslinking contributes to the insolubilization of the polymer. In this way, the marked sensitivity enhancement of a polymer curing system, sensitized with a photobase generator, was achieved by the addition of the base amplifier **4**. Base proliferation may lead to marked improvements in other UV curing systems. Finally, it is anticipated that other types of base-sensitive polymers, irrespective of whether they are of negative-working or positive-working photoresists, would display photosensitivity enhancement on the addition of base amplifiers; thus base amplifiers could be applicable to microlithographic patterning, though optimization is needed.

In conclusion, we propose the concept of base proliferation reactions to improve performances of photopolymer systems based on base-catalyzed transformations. The base proliferation was demonstrated by a base-catalyzed decomposition of carbamate compounds **1a** and **1b** in solution, which resulted in a nonlinear fragmentation to produce aliphatic amine molecules. The carbamate compound **4**, termed a base amplifier, generated the diamine **5**, which improved the photosensitivity of a negative-working photoresist based on PGMA sensitized with a photobase generator.

Experimental Section

1b: Piperidine(1.31 g 15.4 mmol) in diethyl ether (20 mL) was added slowly to an ice-cooled solution of 9-fluorenylmethyl chloroformate (2.00 g, 7.72 mmol) in diethyl ether (50 mL), and the mixture was stirred under cooling for 20 min and at room temperatue for 1.5 h. The solution was washed successively with water, 5 % hydrochloric acid solution, and saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and evaporated to dryness. The solid residue was recrystallized from ethanol to give colorless crystals (0.98 g; 41 %), m.p. 102 – 105 °C. ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 1.55$ (br s, 6H; CH_2), 3.3 – 3.6 (m, 4H; CH_2), 4.1 – 4.5 (m, 3H; CH, CH_2), 7.1 – 7.7 (m, 8H; Ar-H); IR (KBr): $\tilde{\nu} =$ 2936, 1686, 1437, 1259, 1232, 1151, 1106, 762, 739 cm^{-1}; elemental analysis calcd for $C_{20}H_{21}NO_2$ (%): C 78.14, H 6.89, N 4.56; found: C 77.90, H 6.72, N 4.41.

4: A solution of 9-fluorenylmethanol (7.84 g, 40.0 mmol) in dry benzene (60 mL) containing a catalytic amount of di-*n*-butyltin dilaurate (0.1 g) was brought to reflux and treated dropwise with a solution of hexamethylene diisocyanate (3.36 g, 20.0 mmol) in dry benzene (20 mL) under nitrogen. Once the addition was complete, the solution was heated at reflux for 2 h and then cooled to room temperature. The resulting solid precipitate was filtered off and dried in vacuo to give the crude product as a creamy solid. The product was recrystallized from cyclohexanone and washed with acetone to give colorless crystals (10.0 g; 89.3 %), m.p. 175 °C (decomp). ^{1}H NMR (90 MHz, $CDCl_3$): $\delta = 1.0 – 1.7$ (m, 8H; CH_2), 2.9 – 3.4 (m, 4H; CH_2NH), 4.0 – 4.9 (m, 8H; CH, CH_2, NH), 7.1 – 7.9 (m, 16H; Ar-H); IR (KBr): $\tilde{\nu} =$ 3336, 2943, 1685, 1529, 1450, 1259, 1139, 1004, 758, 737 cm^{-1}; elemental analysis calcd for $C_{36}H_{36}N_2O_4$ (%): C 77.12, H 6.47, N 5.00; found: C 77.20, H 6.44, N 4.94.

Base proliferation in solution: The carbamate **1a** (70 mmol dm^{-3}), cyclohexylamine (11 mmol dm^{-3}), and mesitylene as an internal standard were dissolved in 1,4-[D_8]dioxane containing a small amount of tetramethylsilane. The solution was placed in a sealed NMR tube and heated at 100 °C in an oven. The base-catalyzed decomposition of the carbamate compound was monitored by intermittent NMR measurements. The consumption of the carbamate compound was followed by monitoring the decrease of proton signals of the methine and methylene groups, while the formation of dibenzofulvene **2** was followed by monitoring the proton signal of the vinyl group; mesitylene was used as an internal standard.

Sensitivity determination: Photoresist solutions were prepared by dissolving PGMA (0.08 g/1 mL), the photobase generator **3** (10 wt % relative to the polymer), and the base amplifier **4** (2, 4, or 9 wt % relative to the polymer) in 1,1,1,3,3,3-hexafluoro-2-propanol. The solutions were spin-coated on silicon wafers and heated at 110 °C for 60 s to give thin films of 1.1 μm thickness. The thin films were exposed to UV light by using a Hg-Xe lamp without a glass filter, then heated at 110 °C on a hot stage for 15 min. The films were developed with 2-methoxyethyl acetate and the rinse with ethanol. The thickness of residual films was measured to evaluate photosensitivity.

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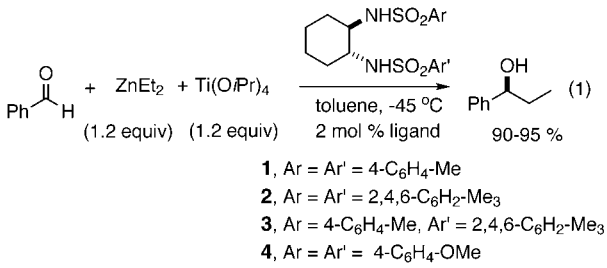

Probing the Conformation of Flexible Catalysts in Solution**

Jaume Balsells, Juan M. Betancort, and Patrick J. Walsh*

Understanding the origins of enantioselectivity in catalytic asymmetric reactions is of special interest because of the magnitude of the impact of enantioselective synthesis on the pharmaceutical industry.[1] However, before delineating the subtle interactions between catalyst and substrate that are responsible for the degree of enantiofacial differentiation, more fundamental questions concerning the operation of the catalyst must be addressed.[2] Knowledge of the parameters which govern the reactivity of the catalyst including the order in the catalyst and reagents, the location of the catalytically active binding site, and the shape of the chiral pocket are essential to relate enantioselectivity data to catalyst – substrate interactions. In catalysts with rigid, well-defined structures possessing limited conformational freedom, such studies are less complicated. However, in many highly enantioselective processes, the chiral environment of the catalyst is dynamic and the enantioselectivities are dependent on the complex interplay of conformational mobility and catalyst – substrate interactions.[2] Herein we examine one such system, the asymmetric addition of alkyl groups to aldehydes with bis(sulfonamide) ligands [Eq. (1)]. We present evidence that indicates that the bis(sulfonamido) ligand adopts a C_2-symmetric conformation in the active form of the catalyst.

The asymmetric addition reaction [Eq. (1)] was developed by Ohno, Kobayashi, and co-workers.[3, 4] Its broad utility and excellent enantioselectivities with a wide range of aldehydes and organozinc reagents were demonstrated by Knochel and co-workers.[5–10] The mechanism of this efficient process was proposed to involve the in situ formation of bis(sulfonamido)titanium complexes.[3, 4, 11, 12] We subsequently reported the synthesis and structures of these species and determined that they perform analogously to the catalyst generated in situ [Eq. (1)].[12] In the solid-state structures of bis(sulfonamido)-titanium complexes complexes (Figure 1), we found that one oxygen atom from each sulfonyl group was coordinated to the titanium center. Coordination of the sulfonyl oxygen atoms to the titanium center could serve to define a more rigid asymmetric environment and may be important in the transfer of asymmetry in the transition state of the asymmetric addition reaction. To explore this possibility, it is necessary to determine the conformation of the bis(sulfonamido) ligand in the active catalyst. Two independent approaches based on structure – enantioselectivity studies were devised to accomplish this goal.

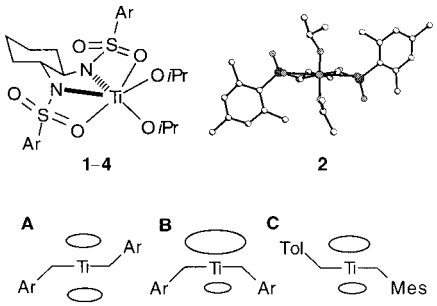

Figure 1. Drawing of the titanium complexes with ligands **1** – **4** (left); the molecular structure with ligand **2** (right) and representations of the titanium complexes with ligands **1** – **4** in the C_2-symmetric *anti* conformation (**A**) and the *syn* conformation (**B**); the pseudo C_2-symmetric conformaton with ligand **3** (**C**).

Two limiting conformations of the bis(sulfonamido) ligand bound to titanium can be envisioned. The first is the C_2-symmetric conformation seen in the crystal structures, where the aryl groups are positioned *anti* to each other (Figure 1, **A**). In the second limiting conformation, the aryl groups are *syn* to each other (Figure 1, **B**, to simplify the discussion, the conformations are abbreviated with line structures). The C_2-symmetric conformation (**A**) has two equivalent binding sites on the titanium center, which are represented by the ovals in Figure 1. In the catalyst formed from ditolyl ligand **1** [Eq. (1)], we would expect these binding sites to be more accessible

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