events. The results of all the inhibition tests are found in Table 1.

In conclusion, by a mix of accident, serendipity and rational design, we have discovered compound **3** which is the most potent small-molecule E-selectin inhibitor to date. Compound **3** can be prepared in ten steps in $>25\%$ overall yield.

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[3] Individual protein–carbohydrate interactions are generally weak ($K_D = 10^{-4}-10^{-3}\,\mathrm{M}^{-1}$); see Y. C. Lee, R. T. Lee, *Acc. Chem. Res.* **1995**, *28*, 321. We determined the sLe^x–E-selectin K_D value to be 1060 μM.

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[10] **3:** MS (70 eV): m/z (%): 713(100) $[M-\mathrm{H}]^-$; ^{1}H NMR (400 MHz, D_2O, 25 °C; selected signals): $\delta = 1.24$ (d, ^3J(H,H) = 6.5 Hz, 3H, H-6 Fuc), 4.76 (q (br), ^3J(H,H) = 6.5 Hz, 1H, H-5 Fuc), 4.84 (d, ^3J(H,H) = 4.0 Hz, 1H, H-1 Fuc), 4.84 (d, ^3J(H,H) = 8.0 Hz, 1H, H-1 Gal), 5.24 (dd, ^3J(H,H) = 9.5/8.0 Hz, 1H, H-2 Gal), 7.50 (t, ^3J(H,H) = 7.5 Hz, 2H, Ar-H), 7.65 (t, ^3J(H,H) = 7.5 Hz, 1H, Ar-H), 8.07 (d, ^3J(H,H) = 7.5 Hz, 2H, Ar-H); **4:** MS (70 eV): m/z (%): 758(100) $[M-\mathrm{H}]^-$; ^{1}H NMR (400 MHz, D_2O, 25 °C; selected signals): $\delta = 1.10$ (d, ^3J(H,H) = 6.5 Hz, 3H, H-6 Fuc), 3.77 (s, 6H, 2 × OCH_3), 4.43 (d, ^3J(H,H) = 8.0 Hz, 1H, H-1 Gal), 4.62 (q (br), ^3J(H,H) = 6.5 Hz, 1H, H-5 Fuc), 4.78 (d, ^3J(H,H) = 4.0 Hz, 1H, H-1 Fuc), 6.95 (s, 2H, Ar-H), 7.08 (s, 1H, Ar-H); **13:** MS (70 eV): m/z (%): 862(100) $[M-\mathrm{H}]^-$; ^{1}H NMR (400 MHz, D_2O, 25 °C; selected signals): $\delta = 1.18$ (d, ^3J(H,H) = 6.5 Hz, 3H, H-6 Fuc), 3.71 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 4.50 (q (br), ^3J(H,H) = 6.5 Hz, 1H, H-5 Fuc), 4.81 (d, ^3J(H,H) = 8.0 Hz, 1H, H-1 Gal), 4.82 (d, ^3J(H,H) = 4.0 Hz, 1H, H-1 Fuc), 5.17 (t (br), ^3J(H,H) = 9.0 Hz, 1H, H-2 Gal), 6.86 (m, 2H, Ar-H), 6.96 (s, 1H, Ar-H), 7.36 (t, ^3J(H,H) = 7.5 Hz, 2H, Ar-H), 7.52 (t, ^3J(H,H) = 7.5 Hz, 1H, Ar-H), 7.87 (d, ^3J(H,H) = 7.5 Hz, 2H, Ar-H); **22:** MS (70 eV): m/z (%): 681(100) $[M-\mathrm{H}]^-$; ^{1}H NMR (500 MHz, D_2O, 25 °C; selected signals): $\delta = 1.16$ (d, ^3J(H,H) = 6.5 Hz, 3H, H-6 Fuc), 4.55 (q (br), ^3J(H,H) = 6.5 Hz, 1H, H-5 Fuc), 4.84 (d, ^3J(H,H) = 8.0 Hz, 1H, H-1 Gal), 4.89 (d, ^3J(H,H) = 4.0 Hz, 1H, H-1 Fuc), 5.16 (dd, ^3J(H,H) = 9.5/8.0 Hz, 1H, H-2 Gal), 7.52 (t, ^3J(H,H) = 7.5 Hz, 2H, Ar-H), 7.65 (t, ^3J(H,H) = 7.5 Hz, 1H, Ar-H), 8.09 (d, ^3J(H,H) = 7.5 Hz, 2H, Ar-H).

[11] Contrary to **12** compound **5**, lacking the electron-withdrawing amide substituent, could be completely debenzoylated to give **20** in $>90\%$ yield applying aqueous NaOH/dioxane at 50 °C.

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[14] Compound **22** was assembled using (R,R)-cyclohexane-1,2-diol and building blocks as those shown in Scheme 2.

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Acids and Bases in One Pot while Avoiding Their Mutual Destruction**

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We have demonstrated recently that separate entrapment in sol–gel matrices of a catalyst and of a reagent which poisons it enables the simultaneous use, in one pot, of these chemicals, which otherwise must be used in consecutive steps.[1] Here we extend the methodology of changing "chemical hostility" into "chemical friendliness" and compatibility, to the classical family of opposing reagents namely acids and bases.

We routinely teach at elementary-level chemistry that since acids and bases annihilate each other when brought together, one needs to separate acidic steps from basic ones in reaction sequences. We show here that sol–gel entrapment[2] solves this problem, and makes it possible to place in one-pot acids and bases without their mutual destruction, while still allowing these reagents to activate or participate in desired reactions. In numerous studies it has been shown that molecules entrapped within sol–gel matrices retain their chemical and physical properties[3] and that external substrate molecules can enter the pore network, react with the dopant, and emerge from the pores as products. Thus, the only

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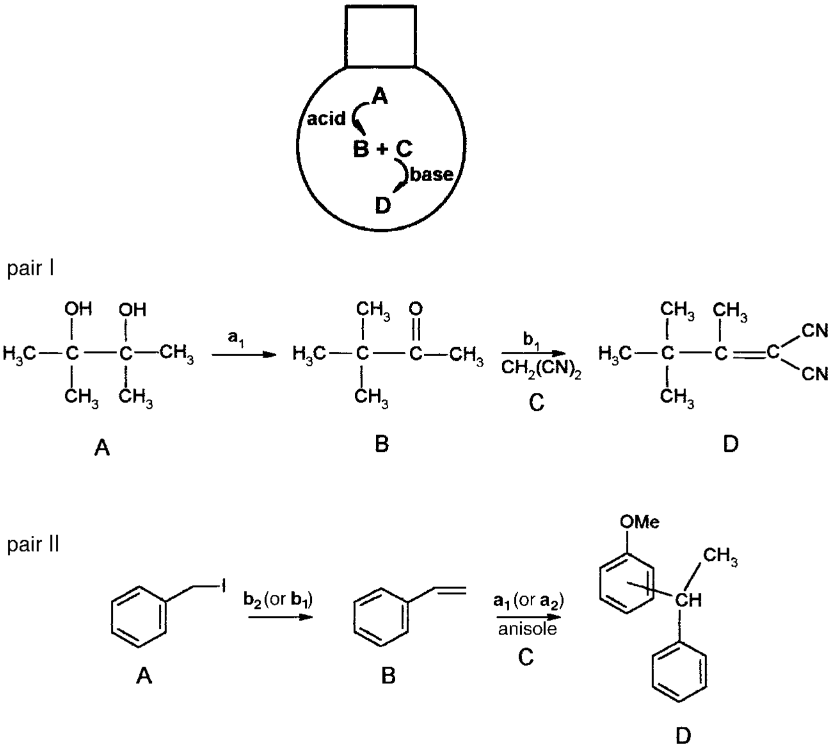
possible reactivity for the dopant is with *diffusable* substrates. For instance, if an acid is entrapped, it can react with a diffusable base and, indeed, one of the more successful applications of doped sol–gel materials has been in the field of pH sensors:[4] here, an entrapped (acidic/basic) indicating molecule reacts with external, diffusable hydronium cations or hydroxyl anions. But then, if the acid and the base are entrapped in two *different* materials, they become, on one hand, protected from each other, and on the other hand, still available for useful reactions. Surface adsorption of acids and bases or derivatization of polymers with acidic/basic moieties leave some of the reagent exposed and consequently acid/base syntheses employing solid-state methods are routinely carried out consecutively.[5] While doped sol–gel materials may contain some of the entrapped molecules at the outer reaches of the particulate or monolithic material, the amount is negligible; there are hundreds of square meters per gram of internal surface area within these porous materials, compared to 1–2 $m^2 g^{-1}$ of external surface. Of relevance to this report are the elegant studies of Pittman and Smith[6] on polymeric bicatalytic systems and the solid-state polymeric transfer of functional groups of Rebek, Jr. et al.[7a] and Cohen et al.;[7b] and studies with oxides, such as alumina, which contain both acidic and basic sites on their surface.[8] These oxides lack, however, the versatility of tailoring the acid/base properties by demand as offered by the ability of sol–gel materials to entrap practically any of the thousands of known acids and bases (except, of course, those which destroy the matrix itself). We demonstrate the approach with various combinations of two acids and two bases, on two pairs of reactions.



Scheme 1. The acids ($\mathbf{a}_1$, $\mathbf{a}_2$) and bases ($\mathbf{b}_1$, $\mathbf{b}_2$) are defined in the text.

The acids were sol–gel (silica, in all cases) entrapped Nafion (perfluorinated resin sulfonic super acid, $\mathbf{a}_1$)[9] and the sol–gel entrapped molybdic acid MO_3–SiO_2 ($\mathbf{a}_2$)[10a] ($H_4SiMo_{12}O_{40}$[10b]). *The bases* were two Ormosils (organically modified silica sol–gel materials), one carrying $H_2N(CH_2)_2NH(CH_2)_3$ functional groups ($\mathbf{b}_1$)[11] and the other guanidine base (1,5,7-triazabicylco[4.4.0]dec-5-ene, TBD) residues ($\mathbf{b}_2$).[12] Thus, three methods for leach-proof entrapments are demonstrated here: the physical entrapment of a polymer, the physical entrapment of an inorganic molecule which strongly associates with the (silanols of the) matrix, and covalent anchoring of small organic molecules. In some reactions the entrapped acids/bases were used as catalysts, while in others as stoichiometric reagents.

The acid/base reaction pairs (Scheme 1) were selected to be corner-stone synthetic steps which are widely used throughout organic and bioorganic chemistry. In pair I (Scheme 1) the first step is a rearrangement reaction catalyzed by an acid, the second step is a carbonyl condensation reaction which requires a base, again as a catalyst. The pinacol–pinacolone rearrangement was used to first convert 2,3-dimethylbutane-2,3-diol into 2,2-dimethylbutan-3-one (Scheme 1) with $\mathbf{a}_1$[13] and the ketone was then condensed with malononitrile in the presence of $\mathbf{b}_1$[14] to $(CH_3)_3CC(CH_3)OHCH(CN)_2$, which dehydrates spontaneously to $(CH_3)_3CC(CH_3){=}C(CN)_2$ (83%). Both $\mathbf{a}_1$ and $\mathbf{b}_1$ are used as catalysts and the ceramic material can be recycled with only minimal loss in activity. We note that consecutive reactions in one pot are possible, naturally in homogeneous systems as well, but with a disadvantage over the heterogeneous procedure we describe herein: in a homogeneous situation, after the first reagent has completed its task, the second reagent has to be added in excess to destroy the first and activate the next step. The sol–gel methodology, on the other hand, allows easy recovery of the reagents or catalysts and their reuse.

With pair II we demonstrated that one can use either the $\mathbf{b}_2$/$\mathbf{a}_1$ combination or the $\mathbf{b}_1$/$\mathbf{a}_2$ combination for the same pair of reactions. The first reaction of pair II was a dehydrohalogenation reaction, which requires a base as a reagent, the second was an aromatic alkylation reaction requiring an acidic catalyst. 2-iodoethylbenzene was dehydroiodinated with $\mathbf{b}_2$ (or $\mathbf{b}_1$)[1] to styrene (Scheme 1), which then alkylated anisole with $\mathbf{a}_1$[15] (or $\mathbf{a}_2$), to 1-(4-methoxyphenyl)ethylbenzene and 1-(2-methoxyphenyl)ethylbenzene in a 5:1 ratio (3.5:1 with $\mathbf{a}_2$). Although the product of the first reaction is the starting materials of the second one, one can put together in the same pot the substrates, the reagent, and the catalyst and allow the reactions to proceed simultaneously; any styrene that forms reacts immediately with the anisole.

Blank reactions were carried out to make sure that the double entrapment is needed. Thus, no reaction was observed when anisole and styrene were treated with entrapped Nafion ($\mathbf{a}_1$) and dissolved TBD (the homogeneous analogue of $\mathbf{b}_2$), which indicates that the base totally quenched the acid. Likewise, the pinacol–pinacolone rearrangement did not take place when $\mathbf{a}_1$ was used with dissolved ethylenediamine (the homogeneous analogue of $\mathbf{b}_1$). Additional blank reactions were the treatment of 2-iodoethylbezene with $\mathbf{a}_1$, which resulted in no reaction,[16] and the treatment of anisole and styrene with undoped silica sol–gel, to ensure that the acidity of the silica does not activate the alkylation reaction (which indeed it does not). Possible leaching was tested by refluxing $\mathbf{a}_1$ or $\mathbf{b}_2$ in benzene for 2 h, followed by extraction with water; the pH of the water was 7 in both cases which indicates that no leaching of the acid or base occured.

In conclusion, we have demonstrated a convenient approach for carrying out different reactions which require acids and bases in one pot. It is a general method, as the accumulated experience with doped sol–gel materials shows that *any* acid or base can be used, and this method leads the way to the simultaneous utilization of many other opposing reagents in various combinations.

Experimental Section

Preparation of the entrapped reagents: Nafion was entrapped in silica sol–gel at 13% (by weight) following the procedure in ref. [9].

Sol–gel entrapment of the molibdic acid: Tetramethoxyorthosilicate (TMOS, 13 mmol), H_2O (0.33 mL, 18 mmol), HCl (0.09 mL; 0.04 M), and MeOH (2 mL, 49 mmol) were stirred at 40 °C for 6 h. To this solution was added a mixture of molibdic acid (0.06 g, 0.37 mmol), NH_4OH (0.1 mL, 25%), and H_2O (2 mL). Gelation occurred within a few minutes. The resulting gel was dried at 180 °C for 16 h, then washed with water, sonicated twice in benzene for 20 min, and then dried again at 180 °C for 6 h, resulting in 0.84 g of the ceramic material. Preparation of the covalently entrapped bases was by the procedures in refs. [11, 12], at a 20% molar loading.

Reaction pair I: $\mathbf{a}_1$ (1.0 g) and $\mathbf{b}_1$ (1.2 g) were suspended in dry benzene (5.0 mL). Pinacol (1.8 g, 1.5 mmol) was added and the mixture was then heated at reflux under N_2 for 30 min. Malononitrile (0.20 g, 3.0 mmol) was then added and the reflux continued for 7 h. Conversion of the pinacol was quantitative (100%), out of which 83% underwent alkylation/dehydration to $(CH_3)_3CC(CH_3){=}C(CN)_2$. A second run with the recovered catalysts resulted in a 76% overall yield.

Reaction pair II, $\mathbf{b}_2/\mathbf{a}_1$ combination: $\mathbf{a}_1$ (1.0 g), $\mathbf{b}_2$ (0.9 g), 2-iodoethylbezene (0.35 g, 1.5 mmol), and anisole (0.16 g, 1.5 mmol) of were placed in dry benzene (5.0 mL) and the mixture heated at reflux under N_2. The reaction was stopped after 4 h at 32% conversion yielding $4\text{-}MeOC_6H_4CH(CH_3)C_6H_5$ and $2\text{-}MeOC_6H_4CH(CH_3)C_6H_5$ in a 5:1 ratio.

The $\mathbf{b}_1/\mathbf{a}_2$ combination: under similar conditions to those above $\mathbf{a}_2$ (0.84 g), $\mathbf{b}_1$ (1.2 g), 2-iodoethylbenzene (0.35 g, 1.5mmol), anisole (0.16 g, 1.5 mmol), 4 h reflux) proceeded as well, although at a lower conversion of 21% with a 3.5:1 product ratio. (It seems that the base $\mathbf{b}_2$ is superior to $\mathbf{b}_1$ because the latter may undergo some competitive N alkylation). All products in this report are known and were identified and characterized by standard techniques (NMR spectroscopy, gas chromatography (GC), and GC-mass spectrometry (GC-MS)).

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Photonic Transduction of a Three-State Electronic Memory and of Electrochemical Sensing of NADH by Using Surface Plasmon Resonance Spectroscopy**

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Signal-triggered switching of the functionalities of molecular,[1, 2] macromolecular,[3] or biomolecular systems[4, 5] has been suggested as a means to develop chemistry-based memory devices. Photonic,[6] electrochemical,[7] magnetic,[8] pH,[9] or thermal signals[10] can be used to switch molecular redox or optical functions. Phase transitions or random-coil/helix transformations of polymers are stimulated by temperature,[11] pH,[12] chemical,[13] electrical,[14] and photonic signals.[15] Similarly, enzyme transformations,[16] substrate–receptor complexes,[17] or double-stranded DNA interactions[18] are switched by photonic signals. The conversion of "ON"–"OFF" switchable chemical functionalities into memory devices requires, however, the integration of the chemical systems with surfaces such that the triggered functionality and the recorded information are transduced, without erasure of the encoded information. Advances in the field demonstrated the electronic transduction of photonically activated molecular redox functions on electrodes[19] or light-stimulated bioelectrocatalytic transformations on electrodes,[20] and also,

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