d, 1 H, BrCH), 7.6 (m, 3 H, phenyl-*H*), 8.1 (m, 2 H, phenyl-*H*). Anal. Calcd for $C_{12}H_{17}Br_3O_2SSi$: C, 29.23; H, 3.47. Found: C, 29.42; H, 3.37.

2-Bromo-3-[dibromo(phenylsulfonyl)methyl]norbornane (9). Recrystallization of the concentrate from thermolysis of norbornene and **1** yielded **9** (2.45 g, 98%), white crystals: mp 170–173 °C; IR (cm^{-1}, KBr) 1580 (phenyl, m), 1320 (SO_2 asym stretch, s), 1150 (SO_2 sym stretch, s); ^1H NMR ($CDCl_3$) δ 1.2–1.7 (m, 4 H at C_5 and C_6), 2.0–2.3 (m, 2 H at C-1 and C-4), 2.5 (br, 1 H at C-7), 2.6 (d, 1 H at C-7), 2.8 (br, 1 H at C-3), 4.2–4.3 (m, 1 H at C-2), 7.6 (m, 3 H, phenyl-*H*), 8.2 (m, 2 H, phenyl-*H*). Anal. Calcd for $C_{14}H_{15}Br_3O_2S$: C, 34.52; H, 3.10. Found: C, 34.33, H, 3.20.

The photolysis experiment (4 h) gave **9** (95%), identical with that obtained thermally.

Dibromo(2-bromocyclopentyl)methyl Phenyl Sulfone (10). The concentrate of the photolysis (8 h) product from cyclopentene and **1** yielded **10** (~90%) and **1** (~10%). Chromatography and crystallization afforded **10** (3.9 g, 83%), white crystals: mp 93.5–94 °C; IR (cm^{-1}, KBr) 1580 (phenyl, m), 1350 (SO_2 asym stretch, s), 1150 (SO_2 sym stretch, s); ^1H NMR ($CDCl_3$) δ 1.9–2.3 (m, 6 H, cyclopentyl *H*), 3.5 (m, 1 H, $HCCBr_2SO_2$), 4.7 (m, 1 H, HCBr), 7.6 (m, 3 H, phenyl-*H*), 8.2 (m, 2 H, phenyl-*H*). Anal. Calcd for $C_{12}H_{13}Br_3O_2S$: C, 31.26; H, 2.84. Found: C, 31.42; H, 2.86.

The crude product from the thermal reaction (24 h) contained **1** (~30%), **10** (~50%), and **13** (~20%) and gave **10** (44% conversion, 63% yield) after final crystallization.

Photolysis of 1 in Cyclohexene. A mixture of **1** (2 g, 5 mmol), cyclohexene (18 mL, 14.6 g, 17.7 mmol), and benzene was irradiated at 4 h at room temperature. Concentration gave a pale yellow oil (1.97 g). Chromatography of the product on silica gel with hexane as eluent yielded a mixture of (1) 3-bromocyclohexene (**14**; ~10%) [^1H NMR ($CDCl_3$) δ 1.3–2.4 (m, 6 H, on $CH_2CH_2CH_2$), 4.7 (m, 1 H, CH=CBr) and 5.8 (m, 2 H, CH=CH); MS, *m/e* calcd for C_6H_9Br 161.042, found 161.263] and (2) 3-(1-cyclohexenyl)-cyclohexane (**16**, ~40%) [^1H NMR ($CDCl_3$) δ 1.5–2.5 (m, 15 H, methylene and methyne *H*), 5.85 (m, 3 H, *CH*=*CHCHC*=*CH*); MS, *m/e* calcd for $C_{12}H_{18}$ 162.176, found 162.139]. Further elution of the chromatographic column gave dibromomethyl phenyl sulfone (**13**, ~50%, identical with an authentic sample) and initial **1** (~50%).

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Registry No. **1**, 17025-47-7; **3**, 3112-85-4; **4b**, 111-66-0; **4c**, 754-05-2; **5a**, 101166-53-4; **5b**, 101166-54-5; **5c**, 101166-56-7; **9**, 101166-56-7; **10**, 101166-57-8; **14**, 1521-51-3; 2-methyl-1-butene, 563-46-2; norbornene, 498-66-8; cyclopentene, 142-29-0; cyclohexene, 110-83-8.

An Improved Preparation of Benzhydrylamine Resin

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Since its introduction[1] benzhydrylamine resin has proven a valuable polymeric support for the solid-phase synthesis of many physiologically important peptide amides including vasoactive intestinal peptide,[2] substance P,[3] and luteinizing hormone releasing factor.[4] Use of this resin provides the desired peptide α-carboxamide directly upon treatment of the protected peptide–resin with anhydrous hydrogen fluoride. In addition, benzhydrylamine resin has been used for the preparation of more acid-resistant supports to minimize peptide–resin acidolysis[5] as well as photolabile supports for the synthesis of protected peptide fragments.[6]

Table I. Extent of Substitution (1 → 7) as a Function of Various Lewis Acids[a]

Lewis acid	substitution, mmol of N/g of resin[b]
$AlCl_3$	0.00
$FeCl_3$	0.60
CuCl	0.00
$ZnCl_2$	0.09
$SbCl_5$	0.36
$SnCl_4$	0.92

[a] All reactions were performed once on 1 g of styrene–1% divinylbenzene copolymer resin, 4 mmol of the Lewis Acid, and 2 mmol of *N*-(α-chlorobenzyl)phthalimide in 25 mL of 1,2-dichloroethane for 2 h at room temperature. [b] Determined by elemental nitrogen analysis.

In the recommended[7] synthesis of benzhydrylamine resin **3** from poly(styrene-*co*-divinylbenzene) resin **1**, Figure 1, the reductive amination of the intermediate phenyl ketone resin **2** is difficult to force to completion and typically proceeds in 45–55% yield even with low substitutions of benzoyl groups.[8] Both steps are sensitive to reaction conditions, making it difficult to control the extent of final substitution and resulting in a resin that contains substantial amounts of extraneous functionality. A recent report has described the preparation of benzhydrylamine resin from lithiated polystyrenes **4** and *N*-(trimethylsilyl)phenylmethanimine.[9] Due to the regioselectivity of the lithiation this route produces mainly the meta-substituted resin **5**. The rate of acid-catalyzed cleavage of the peptide amide from benzhydrylamine resin is likely to be proportional to the stability of the resultant carbonium ion on the polymer. This resin, lacking a para substituted alkyl group and therefore incapable of such stabilization may be unsuitable for general solid-phase synthesis.

These shortcomings in the syntheses of benzhydrylamine resin may contribute to the low and variable results occasionally reported for the synthesis of some peptide α-carboxamides[10] on this resin. Because improved preparations of the functionalized solid support can often result in higher yields of purer peptides, we sought a new synthesis of benzhydrylamine resin.

We find[11] direct amidoalkylation to be a reliable and experimentally convenient method of functionalizing cross-linked polystyrene resin. Reaction of *N*-(α-chlorobenzyl)phthalimide (**6**)[12] with polystyrene–1% divinylbenzene copolymer **1** and stannic chloride yields phthalimidobenzyl resin **7**. Of the Lewis acids investigated stannic chloride gave the highest incorporation of phthalimidobenzyl groups into resin **1** as shown in Table

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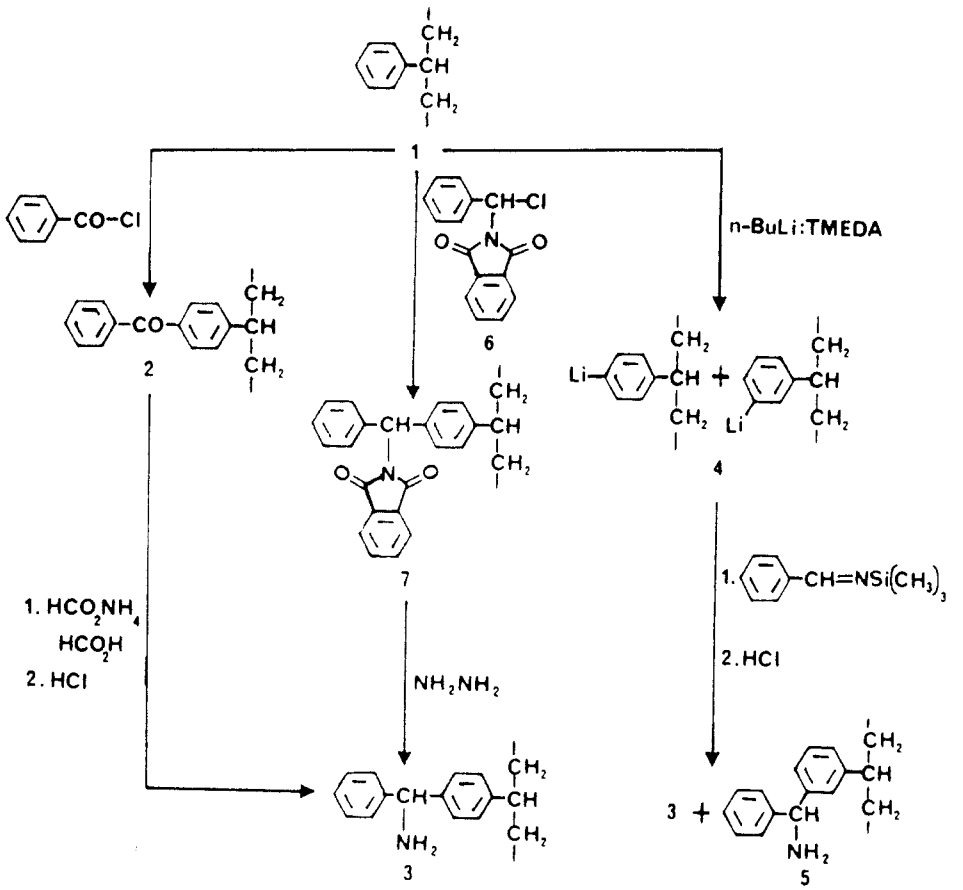

Figure 1. Syntheses of benzhydrylamine resin.

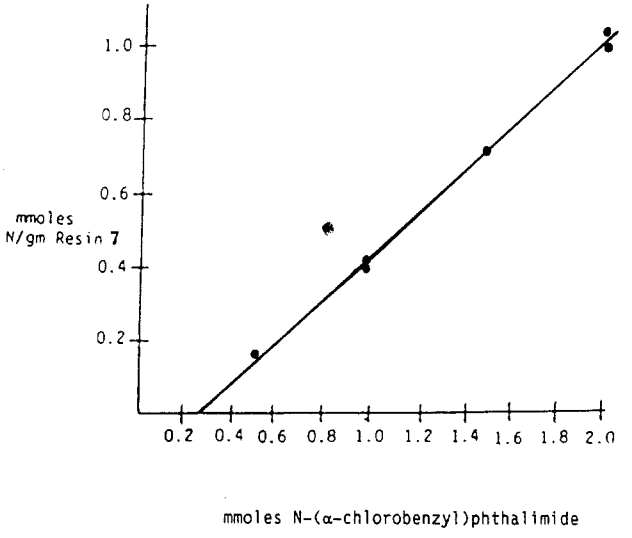

Figure 2. Degree of amidoalkylation as a function of the amount of *N*-(α-chlorobenzyl)phthalimide.

I. Refluxing ethanolic hydrazine readily converts resin **7** to benzhydrylamine resin **3**. The extent of final substitution can be predictably controlled from 0.1 to 1.0 mmol/g resin by varying the amount of **6** as shown in Figure 2.[13] This synthetic route provides benzhydrylamine resin **3** free of any extraneous functionality and at a predetermined substitution.

Experimental Section

Elemental analyses were performed on a Perkin-Elmer 240 apparatus. Infrared spectra were recorded as potassium bromide disks on a Perkin-Elmer 137 spectrophotometer.

Phenylaminomethyl-Polystyrene-1% Divinylbenzene (Benzhydrylamine Resin), Typical Procedure. Washed and dried styrene-1% divinylbenzene copolymer resin (Bio-Rad Laboratories, S-X1, 200-400 mesh beads) was suspended in 1,2-dichloroethane (25 mL/g of resin) containing *N*-(α-chlorobenzyl)phthalimide.[12] A 100% excess of stannic chloride was then added dropwise with vigorous stirring. When the addition was complete the reaction was stirred for 2 h. The mixture was filtered and the resin washed with CH_2Cl_2, ethanol, 1:1 (v/v) ethanol in water, and ethanol and dried in vacuo. The IR spectrum showed phthalimide carbonyl bands at 1710 and 1775 cm^{-1}. The phthalimidobenzyl resin in ethanol (20 ml/g of resin) containing 10% hydrazine was refluxed overnight. The reaction was filtered hot and the resin washed with five portions of hot ethanol and five portions of hot methanol and dried in vacuo. The IR bands at 1710 and 1775 cm^{-1} were absent.

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(13) In those cases investigated the final substitution of resin 3 has agreed closely with the values obtained for resin 7 both by nitrogen analysis and amino acid analysis.

Regioselective Cleavage of 2-Methyltetrahydrofuran: A Versatile Synthesis of 1-Halo-4-pentanols and 4-Halo-1-pentanols

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Differential Functionalization of small molecules for further manipulation is a frequent requirement in organic synthesis. Recently, as part of a larger synthetic project,

