NMR tube. Chemical shifts (δ) are expressed in ppm. NOE difference spectra were recorded according to the method of Hall and Sanders.[4a]

Homonuclear proton COSY experiments were carried out with the pulse sequence D–$\pi/2$–t_1–Δ_1–$\pi/2$–Δ_2–t_2, where t_1 is the incremental delay, D the recycle delay (1 s), Δ_1 the initial delay (0.025 s), and Δ_2 the refocusing delay (0.025 s). t_1 was incremented 256 times at regular intervals. The digital resolution along both axes was 7.5 Hz/point.

Homonuclear proton 2D–J experiments were carried out with the pulse sequence D–$\pi/2$–$t_{1/2}$–π–$t_{1/2}$–t_2. The initial delay $t_{1/2}$ was incremented 64 times at regular intervals. The digital resolution along f_1 and f_2 axes were 0.4 and 1.9 Hz/point, respectively. In both homonuclear proton COSY and 2D–J experiments sine-bell and sine-square-bell window functions were used along f_1 and f_2 axes, respectively, for resolution enhancement.

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Homolytic Reactions of Phenyl Tribromomethyl Sulfone and Olefins

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During a study of 1,1-elimination of phenyl tribromomethyl sulfone (1) by metals and by organometallic bases in efforts to generate (eq 1) and capture bromo(phenylsulfonyl)methylene (3), addition of 1 to varied olefins was observed.[1] Reactions of 1 with terminal olefins 4 (1) at reflux under nitrogen in benzene or (2) upon irradiation (400-W mercury lamp) in benzene at 20–25 °C have now been found to involve directed homolytic addition to give the corresponding phenyl 1,1,3-tribromoalkyl sulfones (5, eq 2). Thus 2-methyl-1-butene (4a), 1-octene (4b), and vinyltrimethylsilane (4c) are readily converted thermally or photolytically to 5a (93%, 90%), 5b (80%), and 5c (46%, 81%).[2,3] The likely overall mechanism of addition involves homolytic cleavage of a C–Br bond in 1 followed by the chain sequence illustrated (eq 3–4). The free-radical behavior of 1 thus parallels that of various polyhalides (for example, CBr_4, $BrCCl_3$, ICF_3, $SiCl_4$, and SO_2Cl_2, etc.) with olefins.[4] Reaction of 4 with an olefin is the first example of such addition of an α-sulfonyl-α-alkyl free radical to a carbon–carbon doubl bond. All attempts however to effect thermal or photolytic additions of dibromomethyl phenyl sulfone ($C_6H_5SO_2CHBr_2$) to various olefins were unsuccessful.

The strained cyclic olefins, norbornene and cyclopentene, undergo addition of 1 to yield 2-bromo-3-[dibromo(phenylsulfonyl)methyl]norbornane (9, 94–98%) and dibromo(2-bromocyclopentyl)methyl phenyl sulfone (10, 63–83%), respectively. Adducts 9 and 10 are sharp-melting, give only single peaks upon HPLC analysis, and are presumably single enantiomeric pairs. The structures of 9 and 10 as anti are suggested by steric considerations, ^{1}H NMR evidence, and the facts that bromotrichloromethane, p-toluenesulfonyl chloride, and 1-iodoperfluoropropane undergo homolytic addition to norbornene in which the trichloromethyl ($Cl_3C\cdot$), the p-toluenesulfonyl (p-$CH_3C_6H_4SO_2\cdot$), and the perfluoro-1-propyl ($CF_3CF_2CF_2\cdot$) radicals attack the carbon–carbon double bond stereospecifically exo.[5] Eclipsing of the bromine (Br) and the

(1) Abstracted from the M.S. Thesis of D. L. Fields, The Ohio State University, Columbus, Ohio, 1984.

(2) Photolyses and thermolyses of 1 in styrene, methyl acrylate, and ethyl vinyl ether, respectively, result in extensive telomerization and polymerization.

(3) Preparative addition reactions of 1 to olefins are simple experimentally and can be followed with ease by monitoring the disappearance of 1 by TLC. Photolysis is of advantage over thermolysis for effecting addition of 1 to low-boiling olefins and in general occurs more rapidly and gives cleaner products. The reaction times vary specifically according to the olefin, the experimental method, and the reactant concentrations. Adducts 5 are usually stable crystalline products which are readily handled. Their structures are assigned from their elemental analyses, from their MS, ^{1}H NMR and IR spectra, and upon consideration of their origins.

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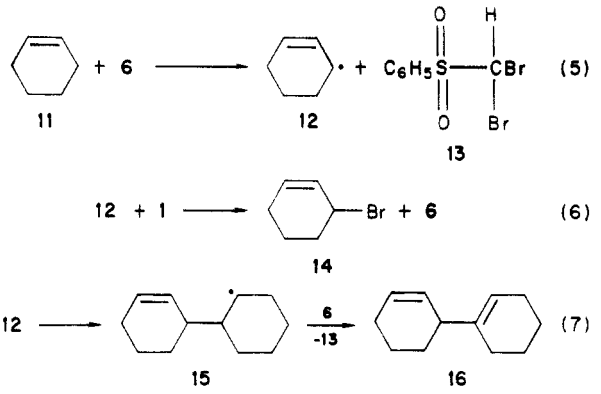
(benzenesulfonyl)dibromomethyl ($CBr_2SO_2C_6H_5$) moieties during transfer as in eq 4 would presumably increase the transition-state energies such that syn additions of 1 to the cyclic olefins are unlikely.

In behavior different from norbornene and cyclopentene, cyclohexene (11) does not undergo addition of 1. Photolysis of 11 and 1 occurs with abstraction of hydrogen by 6 to give the following products: dibromomethyl phenyl sulfone (13, ~50%), 3-bromocyclohexene (14, ~10%), and 3-(1-cyclohexenyl)cyclohexene (16, ~40%).[6,7] The overall reactions of 1 and 11 are illustrated in eq 5–7. Transfer



of hydrogen from an allylic position in 11 to 6 presumably affords the 3-cyclohexenyl radical (12) which abstracts bromine from 1 to form 14 or adds to 11 to yield 15 and then 16 by hydrogen transfer.

(*Z*)- and (*E*)-1-phenylpropenes and allylbenzene also do not undergo addition of 1. Refluxing 1 with the olefins in benzene gives the hydrogen abstraction product 13 quantitatively along with brominated derivatives of the hydrocarbons. Apparently allylic proton abstraction by 6 affording phenylallyl radical ($C_6H_5CH{=}CHCH_2$) is faster than addition to the double bonds of the propenes. Similarly, the internal olefin, 2,3-dimethyl-2-butene, reacts thermally and photolytically with 1 by hydrogen transfer to yield 13 along with non-arylsulfonyl products.

The present study thus reveals that 1 adds readily to terminal alkenes and to the strained cycloalkenes: norbornene and cyclopentene. The efficiency of homolytic addition of 1 to olefins appears to depend on (1) steric factors (accessibility and strain release) in attack of 4 on the double bonds, (2) the rates of competitive allylic proton abstraction by 4, and (3) possibly, the reversibilities of addition of 4 to the unsaturated centers.

Of value also is that 1 may now be synthesized with ease. Previously 1 has been prepared by (1) reaction of sodium (phenylthio)acetate and aqueous sodium hypobromite[8a] and (2) base-catalyzed bromination and cleavage of (phenylsulfonyl)propanone.[8b] In the present work 1 was obtained (98%) conveniently by bromination of methyl phenyl sulfone with aqueous 10% sodium hypobromite in the presence of potassium hydroxide containing a minimal quantity of 1,4-dioxane. Conversion of thiophenol (C_6H_5SH) to methyl phenyl thioether ($C_6H_5SCH_3$), then methyl phenyl sulfone, and finally 1 has been accomplished in 91% overall yield, and purifications within the sequence are unnecessary until final crystallization of 1.

Experimental Section

Phenyl Tribromomethyl Sulfone (1). Potassium hydroxide (75 g, 1.89 mol) in 6 equiv of 10% sodium hypobromite was added in 1 portion to methyl phenyl sulfone (3, 13.7 g, 88 mmol) in 1,4-dioxane (50 mL). After having stirred the mixture at room temperature for 24 h, the crude product was filtered and washed with water (500 mL). Additional product was obtained by diluting the filtrate with water. Recrystallization from 95% ethanol afforded white needles of 1 (33.7 g, 98%): mp 144–145 °C (lit.[8] mp 145 °C);[1] IR (cm^{-1}, KBr) 1592 (phenyl, m), 1344 (SO_2 asym stretch, s), 1164 (SO_2 sym stretch, s); ^1H NMR ($CDCl_3$) δ 7.5–7.8 (m, 3 H, phenyl-*H*), 8.15–8.3 (m, 2 H, phenyl-*H*).

Photolysis of 1 in Olefins in Benzene. General Procedure. Solutions of 1 (4 g, 10 mmol), olefin (4, 40 equiv), and benzene (150 mL) were placed in a photolysis flask equipped with a quartz well, nitrogen inlet, and magnetic stirrer. Irradiations were effected for 3–8 h under nitrogen at room temperature with a 400-W mercury lamp. The reaction mixtures were diluted with ethyl ether (200 mL) and washed with water (100 mL) and saturated brine (100 mL). The solvents were removed in vacuo, and the crude product was analyzed by NMR. The product was crystallized from carbon tetrachloride or chromatographed on silica gel with elution by and then crystallization from carbon tetrachloride.

Thermal Reactions of 1 with Olefins in Benzene. General Procedure. All thermolyses, unless otherwise noted, were conducted by refluxing solutions of 1 (2 g, 5 mmol), olefin (4, 20 equiv), and benzene (30 mL) for 48 h under nitrogen. The mixtures were cooled, diluted with ethyl ether (200 mL), and washed with water (100 mL) and saturated brine (100 mL). The reaction products were concentrated, analyzed, chromatographed, and usually crystallized as described in the above photolysis procedure.

Phenyl 1,1,3-Tribromo-3-methylpentyl Sulfone (5a). The crude product from irradiation (4 h) of 1 and 2-methyl-1-butene was found by NMR to be virtually pure adduct. Recrystallization from carbon tetrachloride afforded **5a** (4.52 g, 90%), white crystals: mp 77–78 °C; IR (cm^{-1}, KBr) 1580 (phenyl, m), 1330 (SO_2 asym stretch, s), 1150 (SO_2 sym stretch, s); ^1H NMR ($CDCl_3$) δ 1.1 (t, 3 H, CH_2CH_3), 2.1 (m, 5 H, $CBr(CH_3)CH_2CH_3$), 3.5 (s, 2 H, $CH_2CBr_2SO_2C_6H_5$), 7.6 (m, 3 H, phenyl-*H*), and 8.2 (m, 2 H, phenyl-*H*); MS, *m/e* (relative intensity) 463 (M^+); mol wt calcd for $C_{12}H_{15}Br_2O_2S$ ($C_{12}H_{15}Br_3O_2S$ - Br·) 383.128, found 382.922. Anal. Calcd for $C_{12}H_{15}Br_3O_2S$: C, 31.13; H, 3.27. Found: C, 32.01; H, 3.23. (Some decomposition of the product occurs while drying at 50 °C for 12 h before elemental analysis).

NMR analysis of the thermolysis product indicated it to be 1 (7%) and **5a** (93%). Chromatography and recrystallization from benzene gave **5a** (2.1 g, 91%), identical with the above product.

Phenyl 1,1,3-Tribromononyl Sulfone (5b). After the reaction mixture had been thermolyzed for 120 h and concentrated, NMR analysis of the crude product revealed the following: 1 (~20%) and **5b** (~80%). Chromatography on silica gel yielded **5b** (1.8 g, 70%) as an oil: IR (cm^{-1}, neat) 1580 (phenyl, m), 1340 (SO_2 asym stretch, s), 1160 (SO_2 sym stretch, s); ^1H NMR ($CDCl_3$) δ 0.7–2.2 (m, 13 H, nonyl *H*), 3.2 (m, 2 H, $CH_2CBr_2SO_2C_6H_5$), 4.4 (m, 1 H, BrC*H*), 7.6 (m, 3 H, phenyl-*H*), 8.2 (m, 2 H, phenyl-*H*); MS, *m/e* calcd for $C_{15}H_{21}Br_3O_2S$ 505.118, found 504.868.

Trimethyl[1,3,3-tribromo-3-(phenylsulfonyl)propyl]silane (5c). Irradiation (3 h), concentraton, and crystallization of the product from vinyltrimethylsilane and 1 gave **5c** (4.06 g, 81%); mp 137–138 °C; IR (cm^{-1}, KBr) 1590 (phenyl, m), 1385 (SO_2 asym stretch, s), 1158 (SO_2 sym stretch, s), 1252 (C–Si sym bending, s), 850 (C–Si rocking, s), 760 (C–Si, rocking, s); ^1H NMR ($CDCl_3$) δ 0.19 (s, 9 H, $(CH_3)_3Si$), 3.1–3.3 (m, 2 H, $CH_2CBr_2SO_2$), 3.6 (d of

(5) For discussion of the stereochemistry of free-radical addition of bromotrichloromethane, *p*-toluenesulfonyl chloride, and 1-iodoperfluoropropane, respectively, to norbornene, see: (a) Davies, D. I. *J. Chem. Soc.* **1960**, 3669–3673. (b) Cristol, S. J.; Reeder, J. A. *J. Org. Chem.* **1961**, *26*, 2182–2185. (c) Brace, N. O. *J. Org. Chem.* **1962**, *27*, 3027–3032. (d) Davies, D. I.; Cristol, S. J. "Advances in Free-Radical Chemistry"; Logos Press Limited; New York, 1965; Vol. 1, pp 155–209. (e) The ^1H NMR of **9** is nearly identical with that of *endo*-2-iodo, *exo*-3-perfluoropropylnorbornane derived from thermal addition of 1-iodoperfluoropropane to norbornene as initiated by azobisisobutyronitrile.[5c] An important structural feature of **9** is that the ^1H NMR of endo-*H* at C-2 of its norbornyl unit is a *triplet* at δ 4.2–4.3 ($CDCl_3$).

(6) Thermolysis of 1 also effects hydrogen abstraction from cyclopentene with formation of **13** (~20%).

(7) In the absence of an olefin, 1 is recovered totally upon refluxing in benzene and in chlorobenzene for long pereiods (~48 h). Loss of bromine and conversion to 1,2-bis(phenylsulfonyl)-1,1,2,2-tetrabromoethane ($C_6H_5SO_2CBr_2SO_2C_6H_5$) thus do not occur. Presumably the (benzenesulfonyl)dibromomethyl radical (**6**) does not form in sufficient quantity under the above conditions to dimerize.

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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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