Amino-Protecting Groups Subject to Deblocking under Conditions of Nucleophilic Addition to a Michael Acceptor. Structure−Reactivity Studies and Use of the 2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonyl (Bspoc) Group

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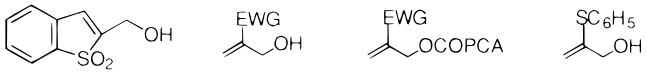
A new type of amino-protecting group is described in which a Michael acceptor is incorporated into the protectant so that treatment with a nucleophile will trigger deblocking. Comparison of various Michael acceptors showed that for several key electron-withdrawing groups, the order of reactivity was $C_6H_5SO_2$ > Me_3CSO_2 > COOEt > C_6H_5SO > $C_6H_4NO_2$-*p*. The reactivity of the nucleophile (e.g., primary and secondary aliphatic amines) followed an order related to both intrinsic basicity and steric effects. *β*-Substituents in the Michael acceptor caused significant retardation of the deblocking process. The Bspoc function was chosen for initial elaboration into a practical system for use in peptide synthesis. Bspoc amino acid chlorides were used as coupling agents and silica-tethered secondary amines as deblocking agents. With the latter, deblocking occurs cleanly and no byproducts remain in the organic solvent in which the deblocking is executed.

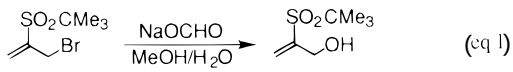
Introduction

Recently a new type of base-sensitive amino-protecting group has been described in preliminary form.[1] In contrast to classical base-sensitive protectants which are deblocked by *β*-elimination reactions, the new groups are deblocked by nucleophilic addition to a Michael acceptor. In the present paper experimental details are presented covering the initial studies which involved (a) basic structure−activity relationships and (b) applications to peptide synthesis in solution via a *β*-unsubstituted analogue of the 1,1-dioxobenzo[*b*]thiophene-2-ylmethyloxycarbonyl (Bsmoc) residue described previously which is based on the cyclic, *β*-phenylated alcohol **1**.

***β*-Unsubstituted Allylic Systems: Structure−Reactivity Effects.** To determine the relative activating effects of various electron-withdrawing groups (EWG), a number of allylic alcohols **2** was synthesized and converted to model urethane derivatives **3** (PCA = *p*-chloroaniline) via reaction with *p*-chlorophenyl isocyanate. Alternatively, an appropriate chloroformate was treated with *p*-chloroaniline to give **3**. Known alcohols (**2**, EWG = $SiMe_3$,[2] COOEt,[3] $C_6H_4NO_2$-*p*[4]) were obtained by published methods. The phenylsulfinyl and phenylsulfonyl alcohols (**2**, EWG = C_6H_5SO, $C_6H_5SO_2$) were readily obtained from sulfide alcohol **4**[5] by *m*-chloroperbenzoic acid (MCPBA) oxidation. The analogous *tert*-butylsulfonyl derivative **6** was obtained by hydrolysis of known bromide **5**[6] via reaction with sodium formate in methanol (60−70%).[7] For comparison of electron-withdrawing groups the *N*-(*p*-chlorophenyl)urethanes **3** were



1 **2** **3** **4**



5 **6** (eq 1)

treated with various primary and secondary amines of varying steric requirements using ^{1}H NMR spectroscopy to monitor the disappearance of the CH_2O protons. Results are collected in Table 1. From the tests with piperidine it is apparent that the *p*-nitrophenyl group is a far less potent activator than any of the groups tested except for the trimethylsilyl residue which did not induce reaction with any of the amines listed or with the stronger base 1,1,3,3-tetramethylguanidine. Only with the highly hindered 2,6-dimethylpiperidine was it possible to distinguish the phenylsulfonyl and *tert*-butylsulfonyl functions for which a slightly greater reactivity for the former was found, in agreement with the finding of McDowell and Stirling[8] that Michael additions to substituted phenyl vinyl sulfones correlated well with the Hammett relationship. Table 1 also demonstrates the importance of steric effects in the amino component of the reaction, with more hindered amines reacting more slowly.[9] All amines listed in Table 1 have comparable basicities (pK_a ∼ 10.6−11) yet differ widely in steric requirements. Urethane **3** (EWG = C_6H_5SO) which incorporates the weakly activating phenylsulfinyl group

(1) Carpino, L. A.; Philbin, M.; Ismail, M.; Truran, G. A.; Mansour, E. M. E.; Iguchi, S.; Ionescu, D.; El-Faham, A.; Riemer, C.; Warrass, R.; Weiss, M. S. *J. Am. Chem. Soc.* **1997**, *119*, 9915.

(2) Wells, G. J.; Yan, T. H.; Paquette, L. A. *J. Org. Chem.* **1984**, *49*, 3604.

(3) Villieras, J.; Rambaud, M. *Synthesis* **1982**, 924.

(4) Wesseln, B. *Acta Chem. Scand.* **1967**, *21*, 718.

(5) (a) Behzadi, A.; Owen, L. N. *J. Chem. Soc., Perkin Trans. 1* **1974**, 25. (b) Jones, D. N.; Cottam, P. D.; Davies, J. *Tetrahedron Lett.* **1979**, *51*, 4977.

(6) Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1985**, 425.

(7) Harris, M.; Bull, M. J. *Synth. Commun.* **1985**, *15*, 1225.

(8) McDowell, S. T.; Stirling, C. J. M. *J. Chem. Soc. (B)* **1967**, 348.

(9) For a study of these steric effects for a variety of primary and secondary amines, see: McDowell, S. T.; Stirling, C. J. M. *J. Chem. Soc. (B)* **1967**, 343.

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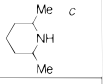
Table 1. Effect of Electron-Withdrawing Group on the Time of Deblocking of 3[a,b]

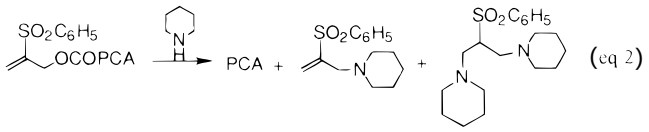
EWG	Time for Complete Deblocking (min)			
			Me_3CNH_2	 [c]
$SO_2C_6H_5$	< 5	< 5	< 5	20
SO_2CMe_3	< 5	< 5	< 5	45
COOEt	< 5	10	21	170
SOC_6H_5	< 5	75	175	inc [d]
$C_6H_4NO_2$-*p*	145	NT	NT	NT
$SiMe_3$	NR	NT	NT	NT

[a] To a solution of 0.18 mmol of urethane in 500 μL of $CDCl_3$ was added 3 equiv of the amine and reaction monitored by loss of the CH_2O signal (60 MHz ^{1}H NMR). [b] NR = no reaction under the conditions given, NT = not tested. [c] Aldrich No. D-18030-0, identified as the *cis*-isomer. [d] Incomplete reaction under the conditions studied.

clearly shows the retarding influence of an increasingly bulky environment around the amino group.

Relative reactivities of the phenylsulfonyl and *tert*-butylsulfonyl urethanes were compared with three other systems bearing base-sensitive amino protecting groups, namely the 2-chloro-3-indenylmethyloxycarbonyl (Climoc),[10] 9-fluorenylmethyloxycarbonyl (Fmoc),[11] and 2-(methanesulfonyl)ethyloxycarbonyl (Msc)[12] analogues, using 3 equiv of piperidine in DCM. All three of these protecting groups undergo deblocking by classic β-elimination reactions. Under conditions which showed no reaction with the Msc derivative, the two α,β-unsaturated sulfonyl derivatives (**3**, EWG = $C_6H_5SO_2$, Me_3CSO_2) showed reactivity comparable to the Climoc derivative whereas the Fmoc analogue was only one hundredth as reactive.

Deblocking byproducts were examined in the case of phenylsulfonyl derivative **7**. Depending on the amount of piperidine used, varying amounts of the mono- and diadducts **8** and **9** were obtained.[13]

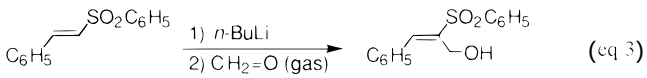


(eq 2)

7 **8** **9**

With 2.3 equiv of piperidine, 69 h were required for conversion of the initially formed monoadduct **8** to **9** whereas with 10 equiv of piperidine, formation of **9** was complete within 15 min.

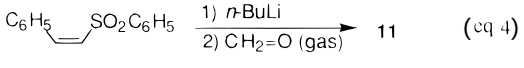
***β*-Substituted Allylic Systems: Steric Retardation.** To examine the effect of β-substitution, a series of urethanes was obtained bearing one or two phenyl substituents at the β-carbon atom. The alcohol **11** was obtained by exploiting Yamamoto's observation that sulfone **10** could be lithiated both regio- and stereoselectively (eq 3).[14]



(eq 3)

10 **11**

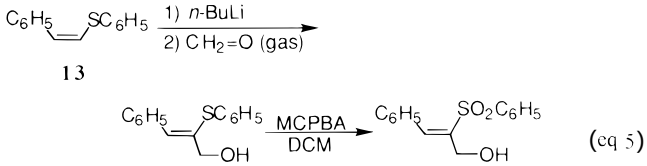
A similar strategy was attempted for the synthesis of the *Z*-isomer, although in this case lithiation of *cis*-sulfone **12** resulted in loss of stereochemistry to give again alcohol **11**. Therefore, the corresponding *cis*-sulfide **13**[15] was first hydroxymethylated and then oxidized to the *Z*-alcohol **15**. IR and NMR spectral data were



(eq 4)

12

consistent with the structural assignments for the two alcohols **11** and **15**.



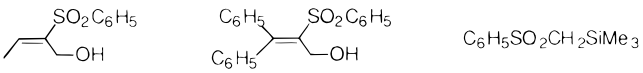
(eq 5)

13 **14** **15**

For comparison with a β-alkyl substituent the methylated sulfone analogous to **11** was also synthesized. Eisch reported that phenyl propenyl sulfone **16** could be lithiated by means of MeLi at −95 °C.[16] In our hands this process was unsuccessful and resulted only in polymerization with either MeLi or *n*-BuLi. However, as

16 **17**

in the case of **15**, the corresponding sulfide **17** was readily lithiated and the derived sulfide alcohol oxidized to sulfone alcohol **18**. Unsaturated sulfide **17** was obtained by base-catalyzed rearrangement of the readily available phenyl allyl sulfide.[17] Finally β,β-diphenyl sulfone alcohol **19** was obtained by standard hydroxymethylation of the corresponding vinyl sulfone which was synthesized from trimethylsilylmethyl phenyl sulfone **20**[18] by treatment of its anion with benzophenone.[19]

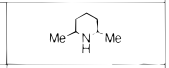
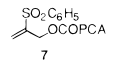
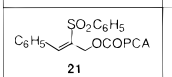
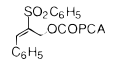
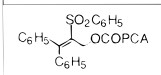


18 **19** **20**

To determine their relative reactivities, urethanes derived from these alcohols were compared with a β-unsubstituted analogue toward three cyclic secondary amines of differing basicities and steric requirements, piperidine, morpholine, and 2,6-dimethylpiperidine (Table 2). Char-

(10) Carpino, L. A.; Cohen, B. J.; Lin, Y.-Z.; Stephens, K. E.; Triolo, S. A. *J. Org. Chem.* **1990**, *55*, 251.
(11) Carpino, L. A. *Acc. Chem. Res.* **1987**, *20*, 401.
(12) Tesser, G. I.; Balvert-Geers, I. C. *Int. J. Pept. Protein Res.* **1975**, *7*, 295.
(13) For prior examples of the formation of such diadducts in related systems, see: (a) Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1984**, *67*, 261. (b) Mitra, S.; Lawton, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 3097.
(14) Yamamoto, M.; Suzuki, K.; Tanaka, S.; Yamada, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1523.
(15) Truce, W. E.; Badiger, V. V. *J. Org. Chem.* **1964**, *29*, 3277.
(16) Eisch, J. J.; Galle, J. E. *J. Org. Chem.* **1979**, *44*, 3279.
(17) Tarbell, D. S.; McCall, M. A. *J. Am. Chem. Soc.* **1952**, *74*, 48.
(18) Craig, D.; Ley, S. V.; Simpkins, N. S.; Whitman, G. H.; Prior, M. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1949.
(19) Ager, D. J. *Chem. Commun.* **1984**, 486.

Table 2. Deblocking of β-Substituted Sulfone Alcohol-Derived Urethanes[a]

Compound	Time for Complete Deblocking (min)		
			
 **7**	< 5	< 5	20
 **21**	< 5	18	NR
 **22**	< 5	38	NR
 **23**	NR	NR	NT

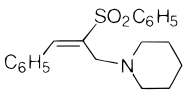
[a] For the method and abbreviations used, see footnotes *a* and *b* of Table 1. For comparison of the urethane of **18** with **22**, see the general procedure described in the Experimental Section.

acterization data for the various urethanes cited in Tables 1 and 2 are given in Table 3.

Although the two mono-β-substituted urethanes **21** and **22** are of comparable reactivity toward piperidine, with the less basic morpholine a significant difference is noticeable. With 2,6-dimethylpiperidine a single β-phenyl substituent renders the system totally unreactive. It is not unusual then that the β,β-diphenylated compound does not react even with piperidine under these conditions.

UV data indicate lesser conjugative interaction between the olefinic linkage and the phenyl substituent in the *Z*-isomer **21** (λ_{max} 267 nm, ϵ = 7500) than in the corresponding *E*-form **22** (λ_{max} 270 nm, ϵ = 18500), suggesting a possible rationale for the greater reactivity of the *Z*-form. The β-methyl-substituted sulfone urethane derived from **18** was less soluble than the phenylated analogue **22**, and therefore the reactivity of these two sulfones was compared at a lower concentration than used for the other compounds in Table 2 (see footnote 1 of Table 2). Under the conditions chosen, **18** was deblocked by morpholine in less than 5 min, whereas **22** required 45 min for complete deblocking. These results are consistent with the smaller size of a methyl group relative to a phenyl group[20] as well as the greater resonance interaction of the olefinic double bond with the phenyl as opposed to the methyl residue.

Piperidine deblocking of **22** gave adduct **24**. Although **24** is formally the product of direct S_N2 displacement at



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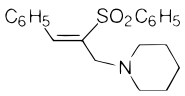

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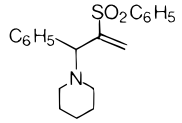
the methylene group of urethane **22**, if this reaction course were followed isomer **21** should yield **25**. In fact, **21** yields exclusively the same amine **24** which was obtained from **22**. Although no mechanistic studies were performed, the results are best explained by Michael attack at the β-carbon atom of both **21** and **22** to give intermediate **26** which is subsequently isomerized to the more stable isomer **24**. In another connection Doomes and co-workers[21] demonstrated that this rearrangement oc-



26

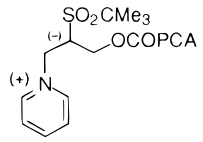
curs readily. Careful monitoring of the reaction by ^{1}H NMR spectroscopy revealed the labile intermediacy of **26** and its conversion to **24**.

Of the various model systems examined, alcohol **6** was most conveniently obtained on a large scale, and therefore the 2-(*tert*-butylsulfonyl)-2-propenyloxycarbonyl (Bspoc) group was chosen for first studies in connection with the testing of Michael-based protective systems in the development of new rapid routes to peptides via solution methods. Upon examining the sensitivity of the Bspoc residue toward conditions pertinent to normal deblocking processes for the currently most common amino-protecting groups, stability was demonstrated to trifluoroacetic acid (TFA) or saturated HCl in HOAc or dimethylamine (DMA)−free *N*,*N*-dimethylformamide (DMF). As expected, deblocking occurs under conditions of catalytic or transfer hydrogenolysis (H_2/Pd−C or NH_4-OCHO/Pd−C). Depending on the conditions, 2-propenyl *tert*-butyl sulfone and/or isopropyl *tert*-butyl sulfone were obtained as byproducts of the hydrogenolysis.

Curious results were observed when Bspoc-PCA **27** was treated with the tertiary base pyridine (2 equiv) in

27 **28** (eq 6)

chloroform solution. The solution became red within 10 min, and after 48 h the urethane was completely consumed. Only PCA (27%) and decarbonylated adduct **28** (60%) were found. Amine **28** could be derived from **27** by base-catalyzed decomposition or via initial pyridine adducts **29** or **30**.



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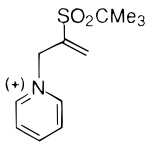

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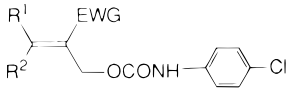
Even in the absence of a base, urethanes such as **27** were found not to be completely stable for long periods. For example a sample of urethane **7** which had been left on the bench for about one year was found to have extruded carbon dioxide to give the 2-phenylsulfonyl analogue of amine **28**. The same conversion was accomplished simply by brief heating of **7** to 130 °C. Although no mechanistic evidence is available, these extrusions can be explained as [3,3] sigmatropic shifts via the enol tautomer of urethane **7**.[22] Although clearly

(20) (a) Eliel, E. L.; Willen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; Table 11.7, p 696. (b) Yashunsky, V. G.; Terentyev, A. P.; Shvedov, V. I. *Zh. Obschch. Khim.* **1995**, *25*, 2457.

(21) Doomes, E.; Clarke, V.; Neitzel, J. J. *J. Org. Chem.* **1987**, *52*, 1540.

Table 3. Characterization of Model Allylic Urethanes Bearing an Electron-Withdrawing Group at the 2-Position[a]

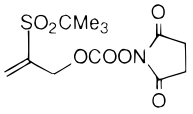


R^1	R^2	EWG	yield, %	mp, °C (recrys solv)	^{1}H NMR, δ[b]	mol formula	analytical data calcd (found) C	H	N
H	H	$SO_2C_6H_5$	71	104−6 (CCl_4)	4.85 (bs,2), 6.15 (bs,1), 6.5 (bs,1), 7.05−8.00 (m,10)	$C_{16}H_{14}ClNO_4S$	54.63 (54.54)	4.01 (3.99)	3.98 (4.05)
H	H	COOEt	65	93−93.5 (CCl_4)	1.25 (t,3), 4.25 (q,2), 4.9 (s,2), 5.9, (bs,1), 6.35 (bs,1), 7.15−7.50 (m,4), 8.0 (bs,1)[c]	$C_{13}H_{14}ClNO_4$	55.04 (54.89)	4.97 (4.69)	4.94 (4.89)
H	H	$SiMe_3$	42	46−47[d]	0.15 (s,9), 4.8 (t,2), 5.5 (m,1), 5.85 (m,1), 7.1−7.5 (m,5)	$C_{13}H_{18}ClNO_2Si$	55.01 (54.80)	6.39 (6.13)	4.93 (4.89)
H	H	$Si(C_6H_5)_3$	84	132−3 (Skelly B/CCl_4)	4.89 (s,2), 5.68 (s,1), 6.06 (s,1), 6.22 (s,1), 7.15−7.7 (m,19)	$C_{28}H_{24}ClNO_2Si$	71.55 (71.51)	5.15 (5.21)	2.98 (2.90)
H	H	SOC_6H_5	69	106−7.5 (CCl_4/SkellyB)	4.65 (s,1), 4.70 (s,1), 6.0 (s,1), 6.3 (s,1), 7.1−7.85 (m,10)	$C_{16}H_{14}ClNO_3S$	57.23 (56.95)	4.20 (4.14)	4.17 (4.10)
H	H	C_6H_4-NO_2-*p*	63	130.5−3.1 (10% EtOAc/ Skelly B)	5.1 (s,2) 5.62 (s,1), 5.74 (s,1), 6.63 (bs,1), 7.28 (m,4), 7.62 (d,2), 8.22 (d,2)	$C_{16}H_{13}ClN_2O_4$	57.76 (57.95)	3.94 (4.03)	8.42 (8.59)
H	C_6H_5	$SO_2C_6H_5$	47	138.5−9.5 (20% EtOAc/ Skelly B)	5.07 (s,2), 6.52 (bs,1), 7.25−8.08 (m,14), 8.15 (s,1)	$C_{22}H_{18}ClNO_4S$	61.75 (61.54)	4.24 (4.27)	3.27 (3.11)
C_6H_5	H	$SO_2C_6H_5$	79	124−125 (15% EtOAc/ Skelly B)	5.23 (s,2), 7.05 (bs,1), 7.22−7.83 (m,15)	$C_{22}H_{18}ClNO_4S$	61.75 (61.70)	4.24 (4.09)	3.27 (3.21)
C_6H_5	C_6H_5	$SO_2C_6H_5$	78	>250 (dec) (95% EtOAc/ EtOH)	5.13 (s,2), 6.8 (bs,1), 6.91−7.58 (m,19)	$C_{28}H_{22}ClNO_4S$	66.73 (66.51)	4.40 (4.44)	2.78 (2.54)
H	CH_3	$SO_2C_6H_5$	58	16.6−8 (30% EtOAc/ Skelly B)	2.27 (d,3), 4.98 (s,2), 6.61 (s,1), 6.75 (q,1), 7.12−8.20 (m,9)	$C_{17}H_{16}ClNO_4S$	55.81 (55.85)	4.41 (4.47)	3.83 (3.83)

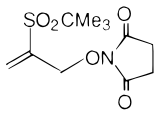
[a] Urethanes were made by reaction of the chloroformate with *p*-chloroaniline or by reaction of *p*-chlorophenyl isocyanate with the corresponding alcohol as described in the Experimental Section for the Bspoc case. [b] Sample dissolved in $CDCl_3$ unless otherwise specified. [c] Sample analyzed in $CDCl_3$−DMSO-d_6. [d] Sample purified by chromatography was used directly for elemental analysis.

of importance with regard to the long-term storage of Bspoc-protected amines, this interesting reaction did not interfere with the use of these intermediates under normal conditions.

Bspoc protection of amino acids was achieved using the chloroformate of **6** in the Bolin technique[23] or via the *tert*-butyl esters of the appropriate amino acids. An alternate general method which is often used for the introduction of protective groups into free amino acids involves an active ester such as **31**.[24] Attempts to synthesize **31** were unsuccessful, only the decarbonylated material **32** being



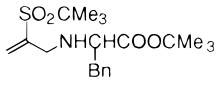
31



32

isolated. This suggests that at some stage the *N*-hydroxysuccinimide anion acts as a potent nucleophilic deblocking agent for the Bspoc residue.

Bspoc amino acids could be converted to their acid chlorides via reaction with thionyl chloride in dichloromethane (DCM) and the acid chlorides used in peptide coupling processes.[25] Generally two-phase couplings were carried out using DCM/H_2O/$NaHCO_3$. Use of a highly reactive acylating reagent such as an acid chloride should guarantee the highest discrimination between reaction at the desired site and at the second electrophilic center, the Michael acceptor. Such premature deblocking processes could lead to the formation of substitution or insertion products. In fact small incursions of such reactions could be observed. Thus treatment of phenylalanine *tert*-butyl ester with Bspoc-Phe-Cl gave the desired dipeptide ester in 94.3% yield. HPLC analysis of the reaction mixture showed 2.09% and 0.32% of two byproducts, which, while not isolated from the reaction mixture, showed HPLC retention times which agreed with those of **33** and **34**, respectively. Authentic samples of **33** and **34** were synthesized, **33** by reaction of Bspoc-



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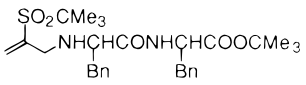
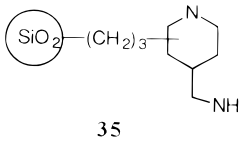


34

Phe-O-*t*-Bu with *tert*-butyl phenylalaninate, and **34** from Bspoc-Phe-Phe-O-*t*-Bu by treatment with a catalytic amount of an aminomethylpiperidinyl silica gel **35**[10] in DCM for a period of 4 days. Amino-loaded silica gel reagents such as **35** and **36** have previously been used



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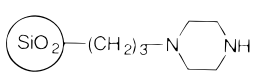

36

for the deblocking of other base-sensitive protecting groups but not always with satisfactory results.[10] They are particularly suited for application to systems which incorporate Michael acceptors such as those described here. An example is provided below.

When Bspoc-Phe-Phe-O-*t*-Bu was deblocked via basic resin **35** (15 equiv of NH per equivalent of the protected

(22) For a related base-catalyzed extrusion, see: Foucaud, A.; El Guemmout, F. *Bull. Soc. Chim. Fr.* **1989**, 405.

(23) Bolin, D. R.; Sytwu, I.; Humiec, F.; Meienhofer, J. *Int. J. Pept. Protein Res.* **1989**, *33*, 353.

(24) Compare: Paquet, A. *Can. J. Chem.* **1982**, *60*, 976.

(25) (a) Carpino, L. A.; Cohen, B. J.; Stephens, K.; Sadat-Aalaee, S.; Tien, J.-H.; Langridge, D. *J. Org. Chem.* **1986**, *51*, 3732. (b) Carpino, L. A.; Beyermann, M.; Wenschuh, H.; Bienert, M. *Acc. Chem. Res.* **1996**, *29*, 268.

dipeptide), HPLC analysis revealed none of the theoretically possible premature product **34**. This result contrasts with that obtained in the case of the simple model **27** which with the same silica reagent (5 equiv of NH per eq. of Bspoc-PCA) led to the formation of 95.1% of PCA and 3.88% of a side product which had the same HPLC retention time as that of **28**. Increasing the ratio of active NH to 15 equiv gave 97.2% of PCA and reduced the amount of material assigned as **28** to 0.55%. For the less reactive piperazino silica reagent **36**,[26] these figures were 7.73% and 0.82%, respectively. With a low molecular weight deblocking base (piperidine) only 0.17−0.18% of **28** was observed with either 5 or 15 equiv of base. Steric factors may play a role in the lesser reactivity observed with the amino acid derivatives versus the simple PCA analogues.

The deblocked free amino dipeptide derived from the silica reagent, being free of any detectable byproducts, was treated directly with a second equivalent of Bspoc-Phe-Cl by the same technique. The resulting tripeptide was obtained cleanly in 75% yield.

Following these preliminary observations Fmoc-protected leucine enkephalin **37**[25a] [Fmoc-Tyr(Bn)-Gly-Gly-Phe-Leu-OBn] was synthesized in a single sequence of steps without isolation of any intermediates. All couplings were carried out via Bspoc amino acid chlorides except for the last, for which Fmoc-Tyr(Bn)-Cl was used. Deblocking was carried out with the aminomethylpiperidine resin.

Substitution of a polymeric active ester for the acid chloride should allow for a complete inverse Merrifield cycle not subject to any of the disadvantages encountered earlier.[10] Protected pentapeptide **37** was obtained in a yield of 59% (crude). The properties of **37** agreed with those previously recorded and catalytic deblocking gave free leucine enkephalin.[27] Gas chromatographic analysis[28] on a chiral column following hydrolysis revealed the absence of racemization (<0.1% D-form) at the Bspoc-introduced phenylalanine residue. This agreed with preliminary racemization studies involving the synthesis of a model dipeptide, Bspoc-Phe-Leu-OMe, and its conversion following deblocking to the corresponding *N*-benzoyl dipeptide methyl ester (<0.1% by HPLC).[29]

Acid chloride couplings were used in the present studies since this work was carried out prior to the discovery of the stability and applicability of Fmoc and other protected amino acid fluorides.[30] Presumably it will be possible to synthesize the Bspoc amino acid fluorides or make use of some of the newer, highly efficient in situ activators[31] directly with the Bspoc amino acids themselves. Indeed the acid fluorides of the related Bs*m*oc amino acids have already been used with good results[1] but so far none of the Bs*p*oc analogues have been tested. Additional solution and solid phase syntheses involving Bspoc chemistry are anticipated for comparison with those previously reported in the Bsmoc case.

Conclusions

It has been shown in this study that urethanes derived from allylic alcohols bearing 2-(alkyl- or arylsulfonyl) residues are, as Michael acceptors, sensitive to the addition of secondary amines at the α,β-unsaturated site. Nucleophilic addition is followed by quick fragmentation to liberate carbon dioxide and the amine built into the urethane unit. The overall process represents a new concept in amino group protection. Structural effects which control the speed of the deblocking step were surveyed. By using a polymeric secondary amine for deblocking, it is possible to scavenge any low molecular weight byproducts generated from the Michael acceptor moiety and simply evaporate the solution to obtain the desired amine. An example of the practical application of such a system to the solution assembly of a simple pentapeptide is described.

Experimental Section

General. Melting points and boiling points were uncorrected. Elemental analyses were carried out by the University of Massachusetts Microanalytical Laboratory under the direction of Greg Dabkowski.

2-(Phenylsulfonyl)-2-propenyl Alcohol. A mixture of 5.03 g (30.3 mmol) of 2-(phenylthio)-2-propenyl alcohol[5] and 12.74 g (62.7 mmol) of 85% *m*-chloroperbenzoic acid in 250 mL of DCM was stirred overnight at room temperature. The mixture was extracted with three 100-mL portions of saturated $NaHCO_3$, followed by 100 mL of water. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C. The residue was chromatographed on silica gel (100−200 mesh, 50 g/gram of compound) with 40% EtOAc/Skelly B as eluent, to give 4.30 g (72%) of the sulfone as a colorless oil; IR (neat) 3500, 1580, 1440, 1300, 1170, 1130, 1050, 950, 900, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.70 (bs, 1), 4.20 (bs, 2), 6.05 (bs, 1), 6.35 (bs, 1), 7.30−7.95 (m, 5). Anal. Calcd for $C_9H_{10}O_3S$: C, 54.53; H, 5.08; S, 16.17. Found: C, 54.57; H, 5.13; S, 16.02.

2-(Methylsulfonyl)ethyl N-*p*-Chlorophenyl Carbamate. A solution of 2.06 g (16.6 mmol) of 2-(methylsulfonyl)-ethyl alcohol and 2.55 g (16.6 mmol) of *p*-chlorophenyl isocyanate in 15 mL of benzene was refluxed for 30 min. The solvent was removed in vacuo from a water bath at 45 °C to give a solid which was recrystallized from $CHCl_3$ to give 2.98 g (65%) of the urethane, mp 147−147.5 °C; IR (KBr) 3360, 1720, 1600, 1490, 1310, 1230, 1130, 1070, 830, 760 cm^{-1}; ^1H NMR (DMSO-d_6−$CDCl_3$) δ 3.0 (s, 3), 3.40 (t, 2,), 4.60 (t, 2), 7.15−7.55 (m, 4), 9.20 (bs, 1). Anal. Calcd for $C_{10}H_{12}ClNO_4S$: C, 43.25; H, 4.36; N, 5.04. Found: C, 43.16; H, 4.14; N, 4.99.

2-(Triphenylsilyl)-2-propenyl *N*-*p*-Chlorophenyl Carbamate. To a stirred solution of 4.55 g (0.012 mol) of (1-bromovinyl)triphenylsilane[32] in 30 mL of dry ether at −24 °C (CCl_4/dry ice) was added dropwise under a nitrogen atmosphere 20.8 mL of 1.20 M n-BuLi (0.024 mol) in hexane. Upon completion of the addition, the yellow mixture was allowed to stir at −24 °C for 90 min. Gaseous formaldehyde, generated by heating paraformaldehyde at 170 °C, was passed through a tube 5 mm in diameter into the reaction mixture with the aid of a slow stream of nitrogen until the yellow color of the solution had disappeared. The reaction mixture was stirred at room-temperature overnight, poured into 50 mL of 5% HCl, and diluted with 50 mL of ether. The aqueous layer was separated, the organic layer was extracted with two 50-

(26) Carpino, L. A.; Mansour, E. M. E.; Knapczyk, J. *J. Org. Chem.* **1983**, *48*, 666.
(27) (a) Carpino, L. A.; Chao, H.-G.; Tien, J.-H. *J. Org. Chem.* **1989**, *54*, 4302. (b) Garbay-Jaureguiberry, C.; Roque, B. P.; Oberlin, R.; Anteunis, M.; Combrisson, S.; Lallemand, J. Y. *FEBS Lett.* **1977**, *76*, 93.
(28) Meienhofer, J. *Biopolymers* **1981**, *20*, 1761.
(29) Carpino, L. A.; Rice, N. W.; Mansour, E. M. E.; Triolo, S. A. *J. Org. Chem.* **1984**, *49*, 836.
(30) (a) Carpino, L. A.; Sadat-Aalaee, D.; Chao, H.-G.; DeSelms, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 9651. (b) Carpino, L. A.; Mansour, E. M. E.; Sadat-Aalaee, D. *J. Org. Chem.* **1991**, *56*, 2611.
(31) (a) Carpino, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 4397. (b) Carpino, L. A.; El-Faham, A.; Minor, C. A.; Albericio, F. *J. Chem. Soc., Chem. Commun.* **1994**, 201. (c) Carpino, L. A.; El-Faham, A. *J. Am. Chem. Soc.* **1995**, *117*, 5401.
(32) Brook, A. G.; Duff, J. M.; Legrow, G. E. *J. Organomet. Chem.* **1976**, *122*, 31.

mL portions of water, dried over $MgSO_4$, filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give a white solid which was recyrstallized from Skelly B to give 2.4 g (61%) of 2-(triphenylsilyl)-2-propenyl alcohol, mp 121 °C; IR (KBr) 3320, 3060, 1420, 1105, 1020, 940, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (s, 1), 4.35 (s, 2), 5.63 (s, 1), 6.24 (s, 1), 7.30−7.70 (m, 15). Without further purification the alcohol was treated with *p*-chlorophenyl isocyanate according to footnote *a* of Table 3 (see Table 3 for characterization data).

2-(*tert*-Butylsulfonyl)-2-propenyl Alcohol (6). A mixture of 8.55 g (35.5 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl bromide[6] and 5.31 g (78.1 mmol) of sodium formate in 150 mL of methanol was refluxed overnight. The solution was allowed to cool and concentrated to 50 mL with the aid of a water aspirator, resulting in the precipitation of excess sodium formate. The residue was diluted with 150 mL of water and extracted with five 50-mL portions of DCM. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C. The crude alcohol was recrystallized from 15% EtOAc/Skelly F to give 4.30 g (68%) of the pure alcohol as a colorless solid, mp 53.5−54.5 °C; IR (KBr) 3470, 3120, 3000, 1450, 1370, 1270, 1095, 1050, 960, 900, 800, 750, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (s, 9), 2.57 (t, 1), 4.56 (d, 2), 6.30 (s, 1), 6.31 (s, 1). Anal. Calcd for $C_7H_{14}O_3S$: C, 47.17; H, 7.92; S, 17.99. Found: C, 47.07; H, 7.95; S, 17.70.

2-(*tert*-Butylsulfonyl)-2-propenyl Chloroformate. To a solution of 6.67 g (37.4 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl alcohol in 27 mL of dry THF at 0 °C was added in one portion 27 mL of phosgene. The solution was stirred for 1 h at 0 °C and allowed to stand at room temperature overnight. Excess phosgene and solvent were removed under reduced pressure with the aid of a water aspirator. Recrystallization from 25% ether/Skelly B gave 8.23 g (91%) of the chloroformate as a colorless solid, mp 56.5−57.7 °C; IR (KBr) 2980, 1755, 1430, 1380, 1290, 1140, 1100, 965, 915, 810, 750, 680, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (s, 9), 5.11 (s, 2), 6.37 (s, 1), 6.47 (s, 1). Anal. Calcd for $C_8H_{13}ClO_4S$: C, 39.92; H, 5.44; S, 13.32. Found: C, 40.10; H, 5.40; S, 13.07.

Representative Example of Urethane Synthesis: 2-(*tert*-Butylsulfonyl)-2-propenyl *N*-(*p*-Chlorophenyl)carbamate. To a solution of 0.24 g (1.0 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl chloroformate in 3 mL of benzene at 0 °C was added dropwise 0.26 g (2.0 mmol) of *p*-chloroaniline in 3 mL of benzene. A white precipitate separated almost immediately. After the addition was complete the mixture was stirred at 0 °C for 10 min and for 2 h at room temperature. The mixture was diluted with 15 mL of benzene and extracted with two 15-mL portions of 5% HCl, followed by 15 mL of water. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C. The crude urethane was recrystallized from 20% EtOAc/Skelly B to give 0.26 g (79%) of the pure urethane, mp 124−125 °C. The same compound was obtained in 85% yield by treatment of 2-(*tert*-butylsulfonyl)-2-propenyl alcohol with *p*-chlorophenyl isocyanate in refluxing benzene; IR (KBr) 3340, 3120, 2980, 1730, 1600, 1490, 1430, 1280, 1210, 1070, 975, 915, 830, 750, 620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4 (s, 9), 4.0 (t, 2), 6.3 (s, 1), 6.35 (s, 1), 7.15−7.5 (m, 5). Anal. Calcd for $C_{14}H_{18}ClNO_4S$: C, 50.68; H, 5.47; N, 4.22. Found: C, 50.46; H, 5.47; N, 4.28.

For other urethanes made similarly, see Table 3.

2-(*tert*-Butylsulfonyl)-2-propenyl *N*-Phenylcarbamate. A solution of 1.24 g (6.96 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl alcohol and 0.83 g (6.97 mmol) of phenyl isocyanate in 10 mL of benzene was treated as described for the *p*-chloro derivative. Recrystallization from 25% EtOAc/Skelly B gave in 70% yield the colorless urethane, mp 138.5−140.0 °C; IR (KBr) 3460, 1740, 1600, 1520, 1450, 1290, 1220, 1110, 1070, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4 (s, 9), 5.0 (t, 2), 6.3 (m, 2), 6.9−7.45 (m, 6). Anal. Calcd for $C_{14}H_{19}NO_4S$: C, 56.55; H, 6.44; N, 4.71. Found: C, 56.27; H, 6.19; N, 4.78.

Bis-2-(*tert*-butylsulfonyl)-2-propenyl Ether. A solution of 11.45 g (0.047 mol) of 2-(*tert*-butylsulfonyl)-2-propenyl bromide and 5.19 g (0.062 mol) of $NaHCO_3$ in 145 mL of 50% acetone/water was refluxed for 60 min. The mixture was allowed to cool to room temperature and extracted with three 75-mL portions of DCM. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C. The residue was recrystallized from 40% benzene/Skelly B to give 6.33 g (75%) of 2-(*tert*-butylsulfonyl)-2-propenyl alcohol, mp 49−51 °C. This sample of alcohol was less pure than that, mp 53.5−54.5 °C, obtained via sodium formate. The crude alcohol was treated with phosgene as described above to give the chloroformate. Three recrystallizations gave 4.64 g (60%) of the chloroformate which still showed a depressed melting point, mp 52−53.5 °C. The impure chloroformate was extracted with 15% ether/Skelly B by means of a Soxhlet extraction apparatus. The residue remaining in the thimble was recrystallized from 50% ether/Skelly B to give 0.28 g (2%) of the ether, mp 99−100 °C; IR (KBr) 2975, 1300, 1280, 1100, 1080, 1000, 945, 765, 750, 715, 695, 670; ^1H NMR ($CDCl_3$) δ 1.4 (s, 18), 4.4 (s, 4), 6.38 (s, 2), 6.43 (s, 2); ^{13}C NMR ($CDCl_3$) δ 144.5 (=CH_2), 132.0 (=C), 69.5 (CH_2O), 60.5 (SO_2CMe_3), 24.0 ($SO_2C(CH_3)_3$). Anal. Calcd for $C_{14}H_{26}O_5S_2$: C, 49.68; H, 7.74; S, 18.94. Found: C, 49.43; H, 7.82; S, 18.68.

(*E*)-3-Phenyl-2-(phenylsulfonyl)-2-propenyl Alcohol (11). To a stirred solution of 2.0 g (8.2 mmol) of *trans*-phenyl β-styryl sulfone in 50 mL of dry THF at −78 °C was added dropwise under a nitrogen atmosphere 6.0 mL (8.4 mmol) of 1.4 M n-BuLi within 5 min. The reddish-purple solution was stirred at −78 °C for 30 min. Gaseous formaldehyde, generated by heating paraformaldehyde at 170 °C, was passed through a tube 5 mm in diameter into the reaction mixture with the aid of a slow stream of nitrogen at −78 °C for 45 min. The mixture was allowed to come to room temperature over a period of 30 min while continuing to pass formaldehyde through the reaction mixture until a pale yellow solution was obtained. The reaction mixture was quenched with 75 mL of 5% HCl and extracted with 50 mL of ether. The organic layer was washed with two 50-mL portions of water, dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give 2.1 g (93%) of the crude alcohol as a brown oil. The oil was flash chromatographed in two 1.05-g batches on silica gel (230−400 mesh, 4 × 19-cm column) with 50% ether/Skelly B as eluent to give a total of 0.99 g (44%) of a light yellow solid, mp 85−87 °C. Recrystallization from 40% ether/Skelly B gave the pure colorless alcohol, mp 88−89 °C; UV (MeOH) λ_{max} = 221 nm, ϵ = 12500, λ_{max} = 270 nm, ϵ = 23500; IR (KBr) 3470, 1625, 1445, 1285, 1145, 1020, 770, 755, 735, 700, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.63 (t, 1), 4.37 (d, 2), 7.27−8.13 (m, 11). Anal. Calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; S, 11.69. Found: C, 65.60; H, 5.12; S, 11.31.

3,3-Diphenyl-2-(phenylsulfonyl)-2-propenyl Alcohol (19). To a stirred solution of 1.25 g (3.90 mmol) of 2,2-diphenyl-1-(phenylsulfonyl)ethene in 20 mL of dry THF at −78 °C was added dropwise under a nitrogen atmosphere 2.8 mL of 1.4 M n-BuLi (3.90 mmol). The dark black solution was stirred at −78 °C for 30 min. Gaseous formaldehyde, generated as noted for the preparation of **11**, was passed through the reaction mixture which was then worked up as noted. The residual oil was flash chromatographed on silica gel (230−400 mesh, 5 × 16-cm column) with 30% ether/Skelly B as eluent to give 0.47 g (34%) of the colorless alcohol. In a melting point capillary the compound does not melt but decomposes above 290 °C with blackening; IR (KBr) 3480, 3040, 1590, 1480, 1440, 1370, 1280, 1130, 1020, 960, 790, 730, 700, 680, 610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.47 (t, 1), 4.61 (d, 2), 6.75−7.58 (m, 15). Anal. Calcd for $C_{21}H_{18}O_3S$: C, 71.98; H, 5.18; S, 9.15. Found: C, 71.97; H, 5.22; S, 9.02.

(*Z*)-3-Phenyl-2-(phenylmercapto)-2-propenyl Alcohol (14). To a solution of 2.0 g (9.4 mmol) of phenyl *cis*-β-styryl sulfide in 25 mL of dry tetrahydrofuran (THF) at −78 °C was added dropwise under a nitrogen atmosphere 6.7 mL (9.4 mmol) of 1.4 M n-BuLi within 5 min. The light yellow solution was stirred at −78 °C for 30 min, treated with gaseous formaldehyde, and worked up as noted above. Flash chromatography on silica gel (230−400 mesh, 4 × 24-cm packed column) with 20% EtOAc/Skelly B as eluent gave 1.1 g (48%) of the alcohol, mp 64.0−65.0 °C; IR (KBr) 3240, 3140, 1580,

1470, 1090, 1070, 1010, 740, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.82 (broad, 1), 4.17 (d, 2), 7.15−7.75 (m, 11). Anal. Calcd for $C_{15}H_{14}OS$: C, 74.35; H, 5.82; S, 13.23. Found: C, 74.35; H, 5.90; S, 13.18.

(*Z*)-3-Phenyl-2-(phenylsulfonyl)-2-propenyl Alcohol (15). A mixture of 0.90 g (3.71 mmol) of (*Z*)-3-phenyl-2-(phenylmercapto)-2-propenyl alcohol and 1.55 g (7.63 mmol) of 85% *m*-chloroperbenzoic acid in 20 mL of DCM was stirred at room-temperature overnight. The mixture was diluted with 40 mL of DCM and extracted with two 25-mL portions of saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give a clear oil. The oil was recrystallized from 20% EtOAc/Skelly B to give 0.72 g (71%) of the sulfone, mp 67.5−69.0 °C; UV (MeOH) λ_{max} = 225 nm, ϵ = 11000, λ_{max} = 270 nm, ϵ = 6500; IR (KBr) 3280, 3180, 1445, 1300, 1150, 1080, 1025, 990, 750, 730, 650, 610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.85 (s, 1), 4.67 (s, 2), 7.21−7.83 (m, 11). Anal. Calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; S, 11.69. Found: C, 65.45; H, 4.97; S, 11.82.

(*E*)-3-Methyl-2-(phenylsulfonyl)-2-propenyl Alcohol (18). To a solution of 1.08 g (7.19 mmol) of *trans*-1-propenyl phenyl sulfide in 15 mL of dry THF at −24 °C was added dropwise under a nitrogen atmosphere 7.6 mL of 1.4 M n-BuLi within 5 min. The light yellow solution was stirred at −24 °C for 30 min and treated with gaseous formaldehyde as noted above except that the temperature was held at −24 °C rather than −78 °C for 90 min. Workup gave an oil which was flash chromatographed on silica gel (230−400 mesh, 4 × 20-cm packed column) with 20% EtOAc/Skelly B as eluent to give 0.28 g (22%) of the alcohol as an oil; ^1H NMR ($CDCl_3$) δ 1.92 (d of t, 4), 4.08 (bs, 2), 6.32 (q of t, 1), 7.25 (bs, 5). Without further purification 0.28 g (1.55 mol) of the sulfide alcohol and 0.65 g (3.20 mmol) of 85% *m*-chloroperbenzoic acid in 10 mL of DCM was stirred at room-temperature overnight. The mixture was diluted with 40 mL of DCM, filtered, and extracted with 50 mL of saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give 0.29 g (88%) of the sulfone alcohol as a clear oil; IR (KBr) 3460, 2920, 1635, 1440, 1290, 1140, 1070, 1000, 840, 720, 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10 (d, 3), 2.88 (s, 1), 4.32 (s, 2), 6.48 (q, 1), 7.28−8.10 (m, 5). Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56.59; H, 5.70; N, 15.10. Found: C, 56.47; H, 5.86; N, 14.89.

General Procedure for Monitoring the Deblocking of Urethanes 3, 7, 21, 22, 23, and 27 by Means of 60 and 200 MHz ^1H NMR. To a solution of 0.18 mmol of the urethane in 500 μL of $CDCl_3$ was added an appropriate amount of amine. The reaction was monitored by the disappearance of the CH_2O protons at 60 MHz. For urethane **22** and that of alcohol **18**, a solution of 0.01 mmol of urethane in 500 μL of $CDCl_3$ was treated with 25 equiv of morpholine. The reaction was monitored by the disappearance of the CH_2O protons at 200 MHz. See Tables 1 and 2.

General Procedure for Monitoring the Deblocking of 2-(*tert*-Butylsulfonyl)-2-propenyl *N*-(*p*-Chlorophenyl)-carbamate by HPLC for the Presence of Premature Deblocked Adduct. To a solution of 2-(*tert*-butylsulfonyl)-2-propenyl *N*-(*p*-chlorophenyl)carbamate in DCM was added an appropriate amount of amine. In the case of silica-based reagents the solution was filtered. For liquid amines the solution was injected directly onto an HPLC column. HPLC analysis was carried out on a Waters Radial Pak 10-μm silica column (0.8 × 10-cm) under the following conditions: 18% 2-propanol in hexane as the mobile phase, flow rate 0.5 mL/min, injection volume 5−10 μL, detector 254 nm, attentuation 0.05, Retention times (min) were 13.0 for **27**, 15.0 for **28**, and 17.8 for *p*-chloroaniline.

***N*-(2-(Phenylsulfonyl)-2-propenyl)piperidine (8).** To a solution of 0.50 g (1.42 mmol) of 2-(phenylsulfonyl)-2-propenyl *N*-(*p*-chlorophenyl)carbamate in 2 mL of DCM was added 0.15 mL (1.1 equiv) of piperidine. The solution was stirred for 5 min, and the solvent was removed in vacuo from a water bath at 45 °C. The residue was chromatographed on silica gel (100−200 mesh, 100 g) with 10% EtOH/Skelly B as eluent to give a solid fraction which was recrystallized from Skelly B to give 110 mg (29%) of the mono adduct as a colorless solid, mp 64−65 °C; IR (KBr) 2940, 1440, 1295, 1130, 955, 740, 685, 660, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (bs, 6), 2.15 (bs, 4), 3.15 (s, 2), 6.0 (t, 1), 6.5 (s, 1), 7.3−8.2 (m, 5). Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.37; H, 7.22; N, 5.28. Found: C, 63.23; H, 6.99; N, 5.41.

1,3-Bis[*N*-(Piperidinyl)]-2-(phenylsulfonyl)propane (9). To a solution of 83.3 mg (0.24 mmol) of 2-(phenylsulfonyl)-2-propenyl *N*-(*p*-chlorophenyl)carbamate in 400 μL of $CDCl_3$ was added 235 μL (10 equiv) of piperidine. Conversion to the diadduct was complete within 15 min. The solution was chromatographed on a preparative TLC plate with 7% EtOH/Skelly B as eluent to give 42 mg (50%) of the sulfone diamine as a colorless solid, mp 113.5−114.5 °C; IR (KBr) 2930, 1440, 1290, 1130, 760, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (s, 12), 2.25 (s, 8), 2.55 (q, 2), 2.85 (q, 2), 3.25 (quintet, 1), 7.4−8.0 (m, 5). Anal. Calcd for $C_{19}H_{30}O_2N_2S$: C, 65.11; H, 8.63; N, 7.99. Found: C, 64.97; H, 8.81; N, 7.84.

Reactivity of 2-(*tert*-Butylsulfonyl)-2-propenyl *N*-Phenylcarbamate toward Catalytic Hydrogenation. To a solution of 0.78 g (2.6 mmol) of Bspoc-NHC_6H_5 in 40 mL of 100% EtOH in a 500-mL pressure bottle was added 120 mg of 10% Pd/C. The pressure bottle was charged with 45 psi of hydrogen and shaken at room temperature for 48 h. The catalyst was filtered and the filtrate diluted with 40 mL of DCM. The organic layer was extracted with two 40-mL portions of 5% HCl. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C. The crude product was bulb-to-bulb distilled in a Kugelrohr apparatus at 80 °C/0.7 Torr to give 0.30 g (60%) of *tert*-butyl isopropyl sulfone; IR (neat) 2980, 1480, 1275, 1110, 1050, 880, 805, 700, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4 (d, 6), 1.42 (s, 9), 3.4 (sept, 1). Anal. Calcd for $C_7H_{16}SO_2$: C, 51.18; H, 9.82; S, 19.52. Found: C, 51.05; H, 9.80; S, 19.11.

***tert*-Butyl *N*-(2-(*tert*-Butylsulfonyl)-2-propenyl)phenylalaninate (33).** A solution of 0.494 g (2.05 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl chloroformate and 0.623 g (2.05 mmol) of *tert*-butyl phenylalaninate hydrophosphite in 20 mL of DCM was stirred with 25 mL of 5% $NaHCO_3$ at room temperature for 3 h. The aqueous phase was separated, and the organic phase was washed with two 25-mL portions of 5% HCl. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give 0.87 g (100%) of an oil, which according to ^1H NMR analysis was essentially pure *tert*-butyl 2-(*tert*-butylsulfonyl)-2-(propenyloxycarbonyl)-L-phenylalaninate. To the oil was added 80 mg (0.36 mmol, 0.18 equiv) of *tert*-butyl phenylalaninate. After standing at room temperature for 48 h, 20 mL of Skelly F was added, and the solvent was removed in vacuo to give a white solid. Recrystallization from 50% Skelly B/Skelly F gave 0.56 g (72%) of the ester as a colorless solid, mp 58.5−59.0 °C; IR (KBr) 3320, 1720, 1365, 1285, 1115, 1095, 740, 715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 9), 1.39 (s, 9), 1.81 (bs, 1), 2.91 (m, 2), 3.34−3.65 (m, 3), 6.05 (s, 1), 6.19 (s, 1), 7.19−7.40 (m, 5); ^{13}C NMR ($CDCl_3$) δ 173.9, 146.0, 137.9, 130.2, 129.9, 128.8, 127.1, 82.1, 62.9, 60.6, 48.5, 40.3, 28.5, 24.0; [α] −11.0° (c = 1, CH_2Cl_2); [α] −12.5° (c = 1, CH_2Cl_2). Anal. Calcd for $C_{20}H_{31}NO_4S$: C, 62.96; H, 8.19; N, 3.67. Found: C, 62.70; H, 8.17; N, 3.59.

2-(*tert*-Butylsulfonyl)-2-propenyl-*N*-*p*-chloroaniline (28). A solution of 0.634 g (1.91 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl *N*-(*p*-chlorophenyl)carbamate and 306 μL (3.82 mmol) of pyridine in 4.2 mL of DCM was allowed to stand for 48 h. The solvent was removed in vacuo from a water bath at 45 °C to give a dark red residue. The residue was flash chromatographed on silica gel (230−400 mesh, 4.5 × 18.0-cm column) with 40% ether/Skelly B as eluent, to give a colorless solid which was recrystallized from 5% EtOAc/Skelly B to give 0.33 g (60%) of the allylamine, mp 127.0−128.5 °C; IR (KBr) 3395, 1600, 1520, 1490, 1280, 1265, 1090, 970, 820, 750, 620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9), 4.20 (bs, 3), 6.15 (s, 1), 6.25 (s, 1), 6.45−7.20 (m, 4); ^{13}C NMR ($CDCl_3$) δ 145.1, 144.5, 130.1, 129.3, 123.1, 114.3, 60.4, 45.6, 23.6. Anal. Calcd for $C_{13}H_{18}ClNO_2S$: C, 54.25; H, 6.30; N, 4.87. Found: C, 54.49; H, 6.22; N, 4.77.

2-(Phenylsulfonyl)-2-propenyl-*N*-*p*-chloroaniline. A neat sample of solid 2-(phenylsulfonyl)-2-propenyl *N*-(*p*-chlorophenyl)carbamate, mp 104−106 °C, was stored in an ordinary vial at room temperature. After about 1 year it was noted that the melting point was lower (mp 69−73 °C). The sample was recrystallized from 70% CCl_4/Skelly B which gave the allylamine, mp 76.5−77.0 °C; IR (KBr) 3400, 1590, 1500, 1440, 1300, 1260, 1170, 1070, 970, 820, 750, 720, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.97 (s, 2), 4.12 (bs, 1), 5.93 (s, 1), 6.41 (s, 1), 6.25−7.02 (m, 4), 7.54−7.92 (m, 5); ^{13}C NMR ($CDCl_3$) δ 147.8, 145.6, 139.4, 134.6, 130.1, 129.7, 128.8, 125.5, 123.5, 114.5, 43.8. Anal. Calcd for $C_{15}H_{14}ClNO_2S$: C, 58.53; H, 4.58; N, 4.55. Found: C, 58.27; H, 4.65; N, 4.57.

***tert*-Butyl 2-(*tert*-Butylsulfonyl)-2-propenylphenylalanylphenylalaninate (34).** A mixture of 300 mg (0.524 mmol) of *tert*-butyl 2-(*tert*-butylsulfonyl)-2-propenyloxycarbonylphenylalanylphenylalaninate and 52 mg (0.1 equiv) of aminomethylpiperidinyl silica gel in 5 mL of DCM was allowed to stand for 4 days. The silica gel was filtered and the solvent removed in vacuo from a water bath at 45 °C. The residue was recrystallized from Skelly B to give 210 mg (84%) of the colorless dipeptide derivative, mp 105.0−106.0 °C; IR (KBr) 3360, 3320, 2980, 1730, 1660, 1290, 1150, 1100, 950, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 9), 1.49 (s, 9), 2.55−3.65 (m, 7), 4.80 (q, 1), 5.85 (s, 1), 6.18 (s, 1), 7.05−7.70 (m, 12); [α] −12.0° (c = 1, $CHCl_3$); [α] −13.2° (c = 1, $CHCl_3$). Anal. Calcd for $C_{29}H_{40}N_2O_5S$: C, 65.88; H, 7.63; N, 5.30. Found: C, 65.66; H, 7.42; N, 5.27.

***N*-[2-(*tert*-Butylsulfonyl)-2-propenyloxy]succinimide (32).** To a stirred solution of 0.25 g (2.17 mmol) of *N*-hydroxysuccinimide and 300 μL (2.15 mmol) of triethylamine in 14 mL of dioxane was added 0.523 g (2.17 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl chloroformate. A precipitate separated immediately. The mixture was stirred for 3.5 h, filtered, and washed with 10 mL of dioxane. The solvent was removed in vacuo to give a white solid which was recrystallized from 40% EtOAc/Skelly B to give 0.58 g (97%) of the oxysuccinimide, mp 159−161 °C; IR (KBr) 2980, 1730, 1480, 1450, 1380, 1295, 1200, 1110, 1000, 910, 830, 810, 750, 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (s, 9), 2.7 (s, 4), 4.8 (s, 2), 6.55 (s, 1), 6.7 (s, 1). Anal. Calcd for $C_{11}H_{17}NO_5S$: C, 47.99; H, 6.22; N, 5.09. Found: C, 48.22; H, 6.29; N, 5.17.

***tert*-Butyl 2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonylphenylalaninate.** To a stirred solution of 0.185 g (0.768 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl chloroformate in 2 mL of benzene at 0 °C was added dropwise a solution of 0.34 g (1.53 mmol) of *tert*-butyl phenylalaninate in 5 mL of benzene. Upon addition, a white precipitate began to separate. The slurry was stirred at room temperature for 30 min, poured into 15 mL of ether, and washed with three 15-mL portions of 5% HCl, and 15 mL of water. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C. The resulting oil was recrystallized from 20% ether/pentane to give 0.23 g (70%) of the colorless ester, mp 67−69 °C; IR (KBr) 3410, 2980, 1715, 1510, 1365, 1290, 1155, 1095, 1060, 940, 750, 700, 625 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (s, 9), 1.50 (s, 9), 3.12 (m, 2), 4.56 (q, 1), 4.90 (s, 2), 5.38 (d, 1), 6.14 (s, 1), 6.29 (s, 1), 7.15−7.40 (m, 5); [α] +25.4° (c = 1, CH_2Cl_2); [α] +30.9° (c = 1, CH_2Cl_2). Anal. Calcd for $C_{21}H_{31}NO_6S$: C, 59.27; H, 7.34; N, 3.29. Found: C, 59.31; H, 7.45; N, 3.23.

2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonylphenylalanine. A solution of 18.6 mmol of *tert*-butyl 2-(*tert*-butylsulfonyl)-2-propenyloxycarbonylphenylalaninate in 36 mL of 50% DCM/TFA was stirred at room temperature for 2 h. Excess TFA and solvent were removed in vacuo from a water bath at 45 °C. The resulting oil was recrystallized from 40% ether/Skelly B to give 6.35 g (91%) of the colorless acid, mp 88.0−89.5 °C; IR (KBr) 3270, 1760, 1690, 1520, 1290, 1200, 1100, 1060, 960, 755, 700, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9), 3.20 (m, 2), 4.75 (q, 1), 4.90 (s, 2), 5.35 (d, 1), 6.15 (s, 1), 6.32 (s, 1), 7.15−7.40 (m, 5); [α] −31.0° (c = 0.5, DMF); [α] −37.5° (c = 0.5, DMF). Anal. Calcd for $C_{17}H_{23}NO_6S$: C, 55.27; H, 6.27; N, 3.79. Found: C, 55.02; H, 6.47; N, 3.71.

2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonylphenylalanyl Chloride. To a stirred solution of 2.50 g (6.77 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyloxycarbonylphenylalanine in 15 mL of dry DCM was added dropwise under a nitrogen atmosphere a solution of 4.9 mL (10 equiv) of thionyl chloride in 10 mL of dry DCM. Upon completion of the addition, the solution was refluxed for 2 h. The solution was cooled to room temperature, and excess thionyl chloride and solvent were removed under reduced pressure with the aid of a vacuum pump. The crude residue was recrystallized from 30 mL of 33% DCM/pentane to give 2.13 g (82%) of the acid chloride, mp 100.0−100.5 °C; IR (KBr) 3400, 1810, 1790, 1720, 1510, 1295, 1250, 1105, 760, 710, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (s, 9), 3.27 (m, 2), 4.88 (m, 3), 5.27 (d, 1), 6.10 (s, 1), 6.27 (s, 1), 7.15−7.45 (m, 5); [α] +15.3° (c = 1, CH_2Cl_2); [α] +18.7° (c = 1, CH_2Cl_2). Anal. Calcd for $C_{17}H_{22}ClNO_5S$: C, 52.64; H, 5.72; N, 3.61. Found: C, 52.32; H, 5.39; N, 3.55.

2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonyl Glycine. A mixture of 3.34 g (13.9 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyl chloroformate and 2.95 g (13.8 mmol) of *tert*-butyl glycinate hydrophosphite in 85 mL of DCM was stirred in the presence of 100 mL of 5% $NaHCO_3$ at room temperature for 4 h. Workup and treatment of the intermediate *tert*-butyl ester with TFA in DCM gave an oil which was recrystallized from 30% EtOAc/Skelly B to give 3.25 g (84%) of the acid, mp 105.0−105.5 °C; IR (KBr) 3355, 1765, 1695, 1560, 1290, 1190, 1100, 1050, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (s, 9), 4.05 (d, 2), 4.94 (s, 2), 5.44 (t, 1), 6.26 (s, 1), 6.33 (s, 1). Anal. Calcd for $C_{10}H_{17}NO_6S$: C, 43.00; H, 6.13; N, 5.01. Found: C, 43.00; H, 6.03; N, 4.97.

2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonyl Glycyl Chloride. Obtained in 91% yield as described for the phenylalanine analogue, mp 61.5−62.5 °C; IR (KBr) 3400, 1800, 1740, 1510, 1280, 1100, 1050, 945, 790, 750, 625 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (s, 9), 4.39 (d, 2), 4.95 (s, 2), 5.57 (bs, 1), 6.25 (s, 1), 6.35 (s, 1). Anal. Calcd for $C_{10}H_{16}ClNO_5S$: C, 40.34; H, 5.42; N, 4.70. Found: C, 40.51; H, 5.30; N, 4.83.

Byproduct Formation during the Preparation of *tert*-Butyl 2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonylphenylalanylphenylalaninate. A solution of 51.5 mg (0.129 mmol) of 2-(*tert*-butylsulfonyl)-2-propenyloxycarbonylphenylalanyl chloride and 39.4 mg (0.130 mmol) of *tert*-butyl phenylalaninate hydrophosphite in 10 mL of DCM was stirred with 20 mL of saturated $NaHCO_3$ at room temperature for 10 min. The aqueous phase was separated, and the organic layer was washed with two 20-mL portions of saturated $NaHCO_3$ and two 20-mL portions of 5% HCl. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C. The crude residue was injected for HPLC analysis. Analysis was carried out on a Waters Radial Pak 10-μm C_{18} reverse phase column (0.8 × 10 cm) under the following conditions: 58% methanol in 0.1% trifluoroacetic acid/water as the mobile phase, flow rate 2 mL/min, injection volume 5−10 μL, detector 254 nm, attenuation 0.05. Four peaks were observed having retention times of 3.1, 4.1, 9.2, and 19.6 min. These peaks were assigned to residual Bspoc-Phe-OH (1.9%), **33** (2.1%), **34** (0.3%), and the desired dipeptide ester (94.3%), respectively.

Lack of Byproduct Formation during the Deblocking of *tert*-Butyl 2-(*tert*-Butylsulfonyl)-2-propenyloxycarbonylphenylalanylphenylalaninate by Means of 4-(aminomethyl)piperidine (4-AMP) Silica Reagent (35). A mixture of 25 mg of Bspoc-Phe-Phe-O-*t*-Bu and 0.436 g (10 equiv) of 4-AMP silica reagent **35** in 2 mL of DCM was stirred for 15 min. The mixture was filtered and injected for HPLC analysis which was carried out on a Waters Radial Pak 10-μm C_{18} reverse phase column (0.8 × 10 cm) under the following conditions: 58% methanol in 0.1% trifluoroacetic acid/water as the mobile phase, flow rate 2 mL/min, injection volume 5−10 μL, detector 254 nm, attenuation 0.05. The free dipeptide was formed in 95% purity with no detectable contamination by **34** (<0.1%).

Continuous Solution Assembly of Fmoc-Tyr(Bn)-Gly-Gly-Phe-Leu-OBn (37). A solution of 0.42 g (1.08 mmol) of Bspoc-Phe-Cl and 0.42 g (1.07 mmol) of H-Leu-OBn·HOTs in

10 mL of DCM was stirred in the presence of 50 mL of saturated $NaHCO_3$ for 15 min. The aqueous phase was separated and the organic layer washed with 25 mL of 5% HCl. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give the crude protected dipeptide which was dissolved in 10 mL of DCM and the solution added to a stirred mixture of 15.0 g (1 mmol NH per gram) of 4-(aminomethyl)piperidine functionalized silica gel, **35**, in 40 mL of DCM. The mixture was stirred for 15 min and filtered, and the silica was washed with three 20-mL portions of DCM. The solvent was removed in vacuo from a water bath at 45 °C to give the free dipeptide. A solution of the free dipeptide and 0.30 g (1.00 mmol) of Bspoc-Gly-Cl in 10 mL of DCM was stirred in the presence of 50 mL of saturated $NaHCO_3$ for 15 min. The aqueous phase was separated, and the organic layer was washed with 25 mL of 5% HCl. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give the crude protected tripeptide [^{1}H NMR ($CDCl_3$) δ 0.92 (d, 6), 1.25−1.80 (m, 12), 3.10 (d, 2), 3.90 (d, 2), 4.58 (q, 1), 4.75 (q, 1), 4.95 (s, 2), 5.20 (s, 2), 5.70 (t, 1), 6.21 (s, 1), 6.30 (s, 1), 6.78 (d, 1), 7.20−7.50 (m, 11)] which was dissolved in 10 mL of DCM and the solution added to a stirred mixture of 15.0 g of **35** (recovered from the run described above) in 40 mL of DCM. The mixture was stirred for 15 min and filtered, and the silica was washed with three 20-mL portions of DCM. The solvent was removed in vacuo from a water bath at 45 °C to give the free tripeptide. A solution of the free tripeptide and 0.30 g (1.00 mmol) of Bspoc-Gly-Cl in 10 mL of DCM was stirred in the presence of 50 mL of saturated $NaHCO_3$ for 15 min. The aqueous phase was separated, and the organic layer was washed with 25 mL of 5% HCl. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give the crude protected tetrapeptide [^{1}H NMR ($CDCl_3$) δ 0.92 (d, 2), 1.35−1.85 (m, 12), 3.14 (d, 2), 3.97 (m, 4), 4.65 (q, 1), 4.85 (q, 1), 4.98 (s, 2), 5.20 (s, 2), 5.98 (t, 1), 6.32 (s, 1), 6.39 (s, 1), 6.92 (d, 1), 7.01 (s, 1), 7.15−7.42 (m, 11)] which was dissolved in 10 mL of DCM and the solution added to a stirred mixture of 15.0 g of **35** (recovered from the run described above) in 40 mL of DCM. The mixture was stirred for 15 min and filtered, and the silica was washed with three 20-mL portions of DCM. The solvent was removed in vacuo from a water bath at 45 °C to give the free tetrapeptide which was stirred with a solution of 0.47 g (0.92 mmol) of Fmoc-Tyr(Bn)-Cl in 10 mL of DCM and 50 mL of saturated $NaHCO_3$ for 20 min. The aqueous phase was separated, and the organic layer was washed with 25 mL of 5% HCl. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give 0.61 g (59%) of the crude protected peptide as a yellow solid. TLC analysis showed that the crude product contained Fmoc-Tyr(Bn)-OH and dibenzofulvene along with the protected pentapeptide. Flash chromatography on silica gel (230−400 mesh, 5 × 15 cm column) with 99% EtOAc/HOAc as eluent gave 0.31 g (30% overall) of the protected pentapeptide as a colorless solid, mp 173−175 °C (lit.[25a] mp 178 °C); ^{1}H NMR ($CDCl_3$) δ 0.82 (s, 6), 1.30−1.80 (m, 3), 2.85−3.20 (m, 4), 4.10 (m, 5), 4.25 (m, 3), 4.70 (m, 2), 4.85 (s, 4), 5.01 (d, 1), 5.25 (bs, 2), 6.75−7.80 (m, 27), 7.90 (bs, 1), 8.17 (bs, 1); [α] −17.1° (c = 0.55, DMF), lit. [α] −16.9° (c = 0.9, DMF), also [α] −19.6° (c = 0.55, DMF).

Leucine Enkephalin. To a solution of 100 mg (0.10 mmol) of Fmoc-Tyr(Bn)-Gly-Gly-Phe-Leu-OBn in 20 mL of 1:1 95% EtOH/EtOAc in a 500-mL pressure bottle were added 50 mg of palladium acetate and 50 mg of 10% Pd/C. The pressure bottle was charged with 45 psi of hydrogen and shaken at room temperature for 24 h. The catalyst was filtered, and the solvent was removed in vacuo from a water bath at 45 °C to give an oil which was triturated with ether and filtered to give 35 mg (58%) of the free pentapeptide, mp 149−152 °C (lit.[33] mp 155−158 °C); [α] −25.8° (c = 0.5, DMF), lit.[34] [α] −26.1 (c = 1.0, DMF). The ^{1}H NMR spectrum was superimposable on that published by Garbay and co-workers[27b] [^{1}H NMR (DMSO-d_6) δ 0.9 (m, 6), 1.45−1.70 (m, 3), 2.6, 2.8, 2.9, 3.1 (m, 4), 3.5 (m, 1), 3.6 (m, 2), 4.1 (m, 1), 4.50 (m, 1). 6.7, 7.0 (d, 4), 7.2 (m, 5), 7.9 (m, 2), 8.2 (m, 1), 8.6 (m, 1)]. For the optically pure amino acid introduced using Bspoc protection (Phe) the standard racemization test using a chiral GC column[28] showed 0.11% of the D-isomer.

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Supporting Information Available: Selected additional experimental procedures for synthesis of methyl, benzyl, and *tert*-butyl esters of Bspoc-substituted amino acid and peptide esters, studies of the stability of the Bspoc residue, and copies of IR and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(33) Anwer, M.; Spatola, A. F. *Synthesis* **1980**, 929.
(34) Plucinski, T.; Kupryszewski, G. *Pol. J. Chem*. **1981**, *55*, 573.