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Solid Phase Approaches to *N*-Heterocycles Using a Sulfur Linker Cleaved by SmI_2

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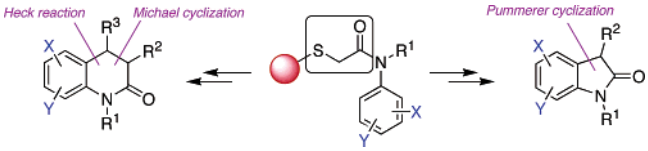

A sulfur HASC (α-hetero-atom substituted carbonyl) linker has been utilized in solid-phase approaches to oxindoles and tetrahydroquinolones. The route to oxindoles employs the first Pummerer cyclizations on solid phase, whereas the route to tetrahydroquinolones involves a microwave-assisted Heck reaction followed by a Michael cyclization. In both cases, the linker is cleaved in a traceless fashion by electron transfer from samarium(II) iodide. The routes illustrate the compatibility of the linker system with a number of reaction types and its utility for library synthesis.

Introduction

Solid-phase synthesis remains an important tool for synthetic organic chemists. The development of versatile linker designs is important for continued advancements in the area.[1] We have previously described a traceless linker strategy for solid-phase organic synthesis where the link to resin is cleaved using samarium(II) iodide (SmI_2).[2] We refer to this family of linkers as HASC (α-hetero-atom substituted carbonyl) linkers (Figure 1). We originally focused on an ether-based HASC linker[3] but have begun to explore the considerable potential of sulfur-based HASC linkers. Sulfur linkers are finding increasing use in phase tag-assisted synthesis,[1c] and we have recently applied a sulfur linker of this type in fluorous phase synthesis.[4] Adjusting the oxidation state of the linking sulfur atom in our solid-phase system allows the use of "classical" organosulfur chemistry to functionalize substrates immobilized using the linker. Here, we describe in full our studies on the solid-phase synthesis of *N*-heterocycles using a sulfur linker cleaved by SmI_2.[5]

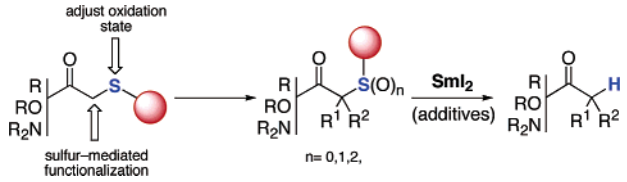

FIGURE 1. A sulfur HASC (α-hetero-atom substituted carbonyl) linker.

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[§] UCB Celltech R&D Ltd.
[||] Pfizer Global Research & Development.

(1) For recent reviews on linkers and cleavage strategies for solid-phase organic synthesis: (a) James, I. W. *Tetrahedron* **1999**, *55*, 4855. (b) Guillier, F.; Orain, D.; Bradley, M. *Chem. Rev.* **2000**, *100*, 2091. (c) McAllister, L. A.; McCormick, R. A.; Procter, D. J. *Tetrahedron* **2005**, *61*, 11527.

(2) For reviews on the use of samarium(II) iodide in organic synthesis: (a) Soderquist, J. A. *Aldrichimica Acta* **1991**, *24*, 15. (b) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29. (c) Molander, G. A. *Org. React.* **1994**, *46*, 211. (d) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307. (e) Molander, G. A.; Harris C. R. *Tetrahedron* **1998**, *54*, 3321. (f) Kagan, H.; Namy, J. L. *Lanthanides: Chemistry and Use in Organic Synthesis*; Kobayashi, S., Ed.; Springer: Berlin, 1999; p 155. (g) Krief, A.; Laval, A.-M. *Chem. Rev.* **1999**, *99*, 745. (h) Steel, P. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727. (i) Kagan, H. B. *Tetrahedron* **2003**, *59*, 10351. (j) Edmonds, D. J.; Johnston, D.; Procter, D. J. *Chem. Rev.* **2004**, *104*, 3371.

(3) (a) McKerlie, F.; Procter, D. J.; Wynne, G. *Chem. Commun.* **2002**, 584. (b) McKerlie, F.; Rudkin, I. M.; Wynne, G.; Procter, D. J. *Org. Biomol. Chem.* **2005**, *3*, 2805.

(4) McAllister, L. A.; McCormick, R. A.; Brand, S.; Procter, D. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 452.

(5) For preliminary accounts of this work, see (a) McAllister, L. A.; Brand, S.; de Gentile, R.; Procter, D. J. *Chem. Commun.* **2003**, 2380. (b) Turner, K. L.; Baker, T. M.; Islam, S.; Procter, D. J.; Stefaniak, M. *Org. Lett.* **2006**, *8*, 329.

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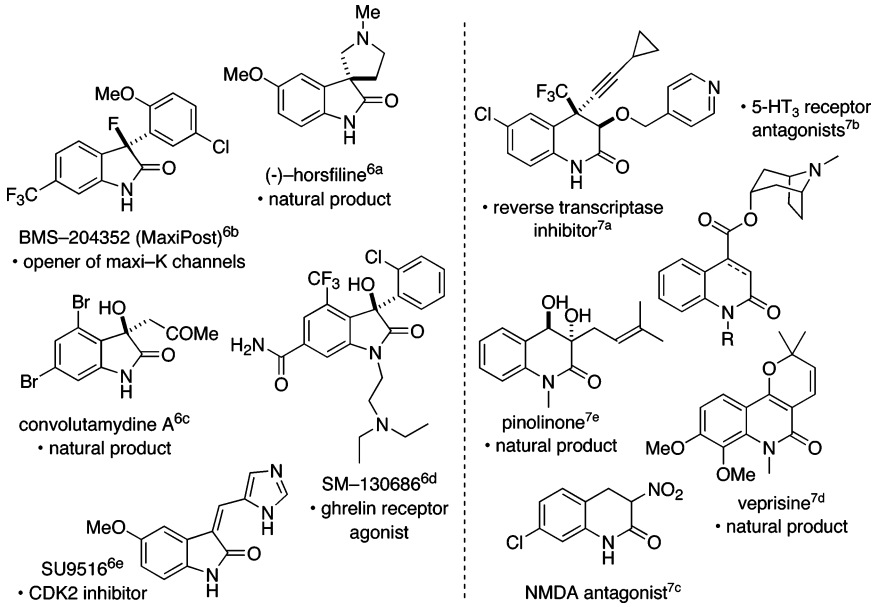


FIGURE 2. The oxindole and tetrahydroquinolone framework.

Our aim was to assess the feasibility of our sulfur linker system and investigate its compatibility with a range of important transformations and reagent systems. We chose to develop a route to oxindoles[6] and tetrahydroquinolones[7] using our linker system. These heterocyclic frameworks can be found in many natural and nonnatural biologically active compounds and are therefore attractive scaffolds for synthesis (Figure 2).[6,7]

Results and Discussion

A Solid-Phase Approach to Oxindoles: Pummerer Cyclizations on Solid Phase. The Pummerer reaction of sulfoxides is a powerful strategy for the efficient synthesis of carbocycles and heterocycles.[8] The α-sulfanyl carbonyl compounds bearing tethered nucleophilic groups undergo cyclization via the formation of reactive sulfonium ions and are of particular synthetic utility.[8] We envisaged that oxidation of the sulfur in α-sulfanyl amides bearing nucleophilic groups, attached to resin via a sulfur atom, followed by sulfonium ion[9] formation would trigger Pummerer cyclization (Figure 3). Crucially, the sulfur link remains intact thus allowing further solid-phase modification steps to be carried out before traceless cleavage of the link using samarium(II) iodide.

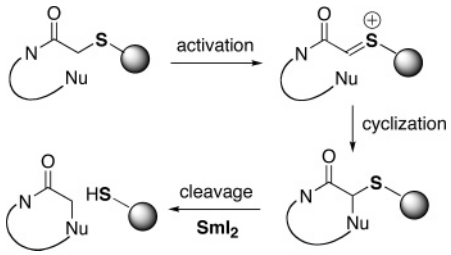


FIGURE 3. Pummerer cyclizations mediated by a sulfur linker.

Applying this approach, we envisaged that simple α-sulfanyl *N*-aryl acetamides **1**, immobilized using our sulfur linker system, could be converted to oxindoles. We chose to establish the sulfur linkage through the reaction of a benzyl thiol resin with α-bromo acetamides. This simple approach would allow access to Pummerer cyclization substrates in a straightforward manner. Benzyl thiol resin **2**[10] was prepared from Merrifield resin by two routes (Scheme 1). Routes via the thiourea[11] and via the thioacetate[10] were found to give similar loadings of *free* "SH" sites.[12]

The feasibility of our solid phase Pummerer approach to oxindoles was initially investigated in solution using benzyl thiol

(6) Jossang, A.; Jossang, P.; Hadi, H. A.; Sévenet, T.; Bodo, B. *J. Org. Chem.* **1991**, *56*, 6527. (b) Shibata, N.; Ishimaru, T.; Suzuki, E.; Kirk, K. L. *J. Org. Chem.* **2003**, *68*, 2494. (c) Kawasaki, T.; Nagaoka, M.; Satoh, T.; Okamoto, A.; Ukon, R.; Ogawa, A. *Tetrahedron*, **2004**, *60*, 3493. (d) Tokunaga, T.; Hume, W. E.; Nagamine, J.; Kawamura, T.; Taiji, M.; Nagata, R. *Biorg. Med. Chem. Lett.* **2005**, *15*, 1789. (e) Li, X.; Huang, P.; Cui, J. J.; Zhang, J.; Tang, C. *Biorg. Med. Chem. Lett.* **2003**, *13*, 1939.

(7) (a) Patel, M.; McHugh, R. J., Jr.; Cordova, B. C.; Klabe, R. M.; Bacheler, L. T.; Ericksen-Viitanen, S.; Rodgers, J. D. *Biorg. Med. Chem. Lett.* **2001**, *11*, 1943. (b) Hayashi, H.; Miwa, Y.; Miki, I.; Ichikawa, S.; Yoda, N.; Ishii, A.; Kono, M.; Suzuki, F. *J. Med. Chem.* **1992**, *35*, 4893. (c) Carling, R. W.; Leeson, P. D.; Moore, K. W.; Smith, J. D.; Moyes, C. R.; Mawer, I. M.; Thomas, S.; Chan, T.; Baker, R.; Foster, A. C.; Grimwood, S.; Kemp, J. A.; Marshall, G. R.; Tricklebank, M. D.; Saywell, K. L. *J. Med. Chem.* **1993**, *36*, 3397. (d) Christopher, E.; Bedir, E.; Dunbar, C.; Khan, I. A.; Okunji, C. O.; Schuster, B. M.; Iwu, M. M. *Helv. Chim. Acta* **2003**, *86*, 2914. (e) Ito, C.; Itoigawa, M.; Otsuka, T.; Tokuda, H.; Nishino, H.; Furukawa, H. *J. Nat. Prod.* **2000**, *63*, 1344.

(8) For recent reviews on the Pummerer reaction see (a) Bur, S. K.; Padwa, A. *Chem. Rev.* **2004**, *104*, 2401. (b) Padwa, A.; Danca, D. M.; Ginn, J. D.; Lynch, S. M. *J. Braz. Chem. Soc*. **2001**, *12*, 571. (c) Padwa, A.; Waterson, A. G. *Curr. Org. Chem.* **2000**, *4*, 175. (d) Padwa, A.; Gunn D. E., Jr.; Osterhout, M. H. *Synthesis*, **1997**, 1353.

(9) Sulfonium ions have begun to find application in solid-phase chemistry. (a) In Pd-catalysed cross-coupling reactions see Vanier, C.; Lorgé, F.; Wagner A.; Mioskowski, C. *Angew. Chem., Int. Ed.* **2000**, *39*, 1679. (b) In cyclopropanations and epoxidations see La Porta, E.; Piarulli, U.; Cardullo, F.; Paio, A.; Provera, S.; Seneci, P.; Gennari, C. *Tetrahedron Lett.* **2002**, *43*, 761. (c) In the Pummerer cleavage of sulfoxide linkers see Rolland, C.; Hanquet, G.; Ducep, J.-B.; Solladié, G. *Tetrahedron Lett.* **2001**, *42*, 7563. (d) Tai, C.-H.; Wu, H.-C.; Li, W.-R. *Org. Lett.* **2004**, *6*, 2905.

(10) Kobayashi, S.; Hachiya, I.; Suzuki, S.; Moriwaki, M. *Tetrahedron Lett.* **1996**, *37*, 2809.

(11) For the preparation of a different thiol resin via a thiourea, see ref 9a.

(12) The loading of *free* SH sites was determined by the immobilization of *N*-methyl-*N*-phenyl α-bromoacetamide, followed by SmI_2 cleavage and isolation/quantification of *N*-methyl-*N*-phenyl acetamide. The discrepancy between the loading obtained by this method and that obtained by sulfur microanalysis (~1 mmol g^{-1}) is presumably due to oxidative cross-linking of the thiol functional groups (See Experimental Section).

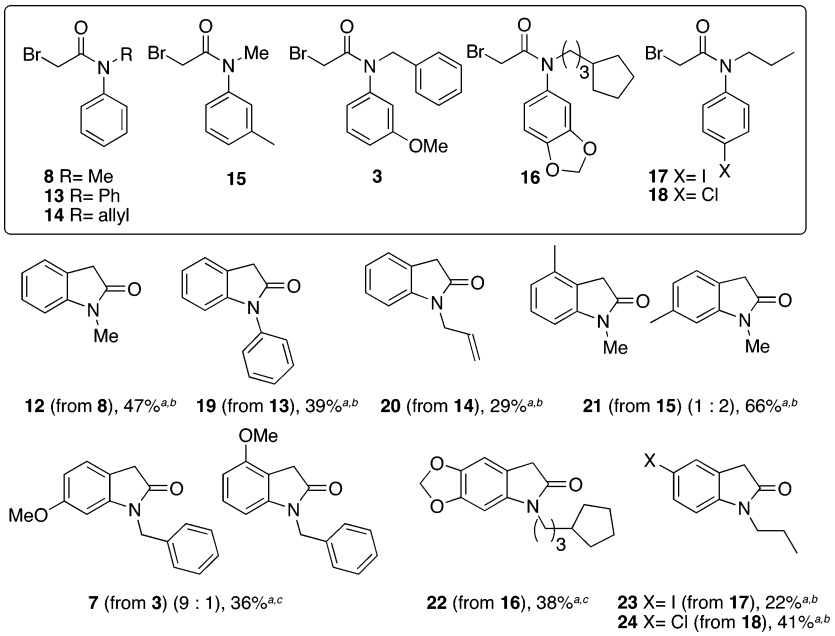
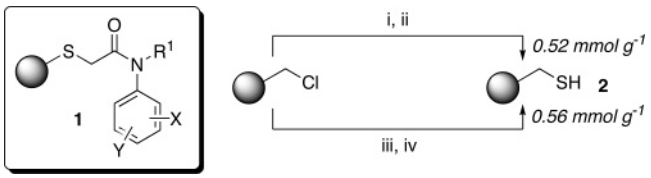


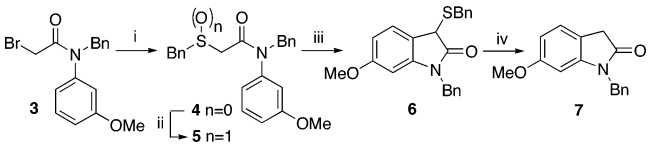
FIGURE 4. Starting materials and oxindole products: (*a*) isolated, overall yields after four steps; (*b*) cyclized using TFAA and $BF_3{\cdot}OEt_2$; (*c*) cyclized using TFAA.

SCHEME 1[a]



[a] Reagents and conditions: (i) $KSC(O)CH_3$, DMF, rt. (ii) $LiBH_4$, THF, rt. (iii) thiourea, DMF, 60 °C. (iv) *n*-$BuNH_2$, DMF, 60 °C.

SCHEME 2[a]



[a] Reagents and conditions: (i) BnSH, NEt_3, DMF, rt, 47%. (ii) HFIP−CH_2Cl_2 (2:1), H_2O_2, rt, 92%. (iii) TFAA, 1,2-dichloroethane, rt, 63%. (iv) SmI_2, DMPU, THF, rt, 48% (unoptimized).

as a model for thiol resin **2**. Thus reaction of α-bromoamide **3**, readily accessible from the corresponding secondary amine and bromoacetyl bromide, with benzyl thiol gave sulfide **4**, which was then oxidized selectively to the sulfoxide **5** using Bégué's H_2O_2 and hexafluoro-2-propanol (HFIP) reagent system.[13] Pummerer cyclization of the electronically activated sulfoxide **5** was readily achieved using trifluoroacetic anhydride.[14] After chromatographic removal of the minor oxindole regioisomer (Figure 4), cleavage of the benzylsulfanyl group from oxindole **6** was carried out using SmI_2 and DMPU (Scheme 2).[3−5]

We next adapted the sequence to solid phase while also assessing the feasibility of carrying out solid-phase Pummerer cyclizations on *unactivated* aromatic substrates. Immobilization of *N*-methyl-*N*-phenyl α-bromoacetamide **8** was achieved by stirring the amide with resin **2** in DMF. The sulfur link in immobilized amide **9** was then oxidized to give sulfoxide **10**. In this electronically unactivated substrate, Pummerer cyclization was found to be most efficiently carried out using stronger activation with TFAA and $BF_3{\cdot}Et_2O$.[14] Cleavage of the sulfur link to resin was then carried out using SmI_2 and DMPU according to our previously reported conditions.[3−5] Pleasingly, oxindole **12** was isolated in high purity and 47% yield after four steps (Scheme 3).

By varying the α-bromoamide used in the sequence, a range of oxindoles has been prepared (Figure 4). As can be seen from the table, neutral, electron rich, and electron-deficient aromatic amide substrates have been employed in the sequence. Interestingly, in the solid-phase synthesis of 5-iodo-1-propyl-1,3-dihydro-indol-2-one **23**, cleavage of the sulfur link to resin can be achieved chemoselectively in the presence of the aryl iodide although the use of excess SmI_2 leads to lower yields through over-reduction. It is known that aryl and alkyl halides can be readily reduced using SmI_2 with additives.[15] Crucially, no aqueous work up is needed after cleavage of the product from resin. In the majority of cases, the products could be separated from DMPU and inorganic byproducts by simple filtration through a short pad of silica after which they were found to give satisfactory ^1H and ^{13}C NMR spectra. Routine chromatography was used for the few examples where minor uncharacterized byproducts were obtained. The structure of the major regioisomer of **7** was confirmed by X-ray crystallography.[16]

As the sulfur link to resin remains intact after the Pummerer cyclization, further modification on resin can allow access to elaborated heterocyclic frameworks. By way of illustration,

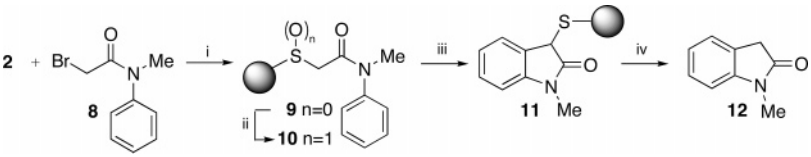
(13) Ravikumar, K. S.; Bégué, J−P.; Bonnet-Delpon, D. *Tetrahedron Lett.* **1998**, *39*, 3141.

(14) It has been noted that $BF_3{\cdot}OEt_2$ is not required for the cyclization of electronically activated systems: (a) Shinohara, T.; Takeda, A.; Toda, J.; Ueda, Y.; Kohno, M.; Sano, T. *Chem. Pharm. Bull.* **1998**, *46*, 6, 918. (b) Saitoh, T.; Ichikawa, T.; Horiguchi, Y.; Toda, J.; Sano, T. *Chem. Pharm. Bull.* **2001**, *49*, 8, 979.

(15) Aryl and alkyl halides can be readily reduced using SmI_2 with additives such as HMPA: Inanaga, J.; Ishikawa, M.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485.

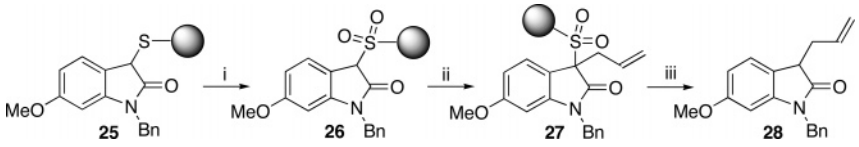
(16) See Supporting Information for the X-ray structure of the major isomer of **7** (CCDC 601447).

SCHEME 3[a]



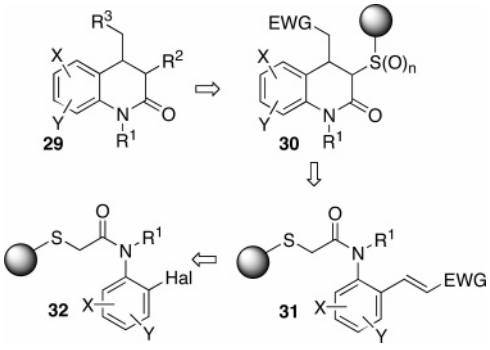
[a] Reagents and conditions: (i) NEt_3, DMF, rt. (ii) HFIP−CH_2Cl_2 (2:1), H_2O_2, rt. (iii) TFAA, $BF_3{\cdot}OEt_2$, 1,2-dichloroethane, rt. (iv) SmI_2, DMPU, THF, rt, 47% isolated yield after four steps on resin.

SCHEME 4[a]



[a] Reagents and conditions: (i) oxone, DMF:H_2O (4:1), rt. (ii) K_2CO_3, KI, allyl bromide, DMF, 60 °C. (iii) SmI_2, DMPU, THF, rt, 30% overall yield for six steps on resin (9:1 mixture of regioisomers, major shown).

SCHEME 5[a]



[a] EWG = electron-withdrawing group.

oxidation of resin-bound oxindole **25** gave sulfone **26**, and alkylation then gave allylated sulfone **27**. Thus the approach proceeds with assistance from the sulfur link in two different oxidation states. Cleavage of the link with SmI_2 and DMPU gave the expected product **28** as a 9:1 mixture of regioisomers in 30% overall yield (Scheme 4). As expected, cleavage of the sulfur linker at the sulfone oxidation state was found to proceed more rapidly than cleavage of the analogous sulfide linkages although yields were found to be similar.

A Solid-Phase Approach to Tetrahydroquinolones. Our proposed, solid-phase approach to tetrahydroquinolones using the sulfur linker is outlined in Scheme 5. Heck reactions of immobilized aryl halides **32** with electron-deficient alkenes should allow access to key intermediates **31**. Base-mediated cyclization will then furnish the tetrahydroquinolone core **30** which can be modified before cleavage from the support.

We began our studies by evaluating the route using a solution phase model system. α-Sulfanyl amides **33** and **34**, in which the benzyl sulfanyl group mimics a benzylic sulfur resin, were prepared. Although few Heck reactions of *N*-α-halophenylamides and carbamates have been reported,[17] both **33** and **34** underwent efficient Heck coupling in *o*-xylene with *tert*-butyl acrylate under microwave conditions. Oxidation of **35** and **36** to the corresponding sulfones and treatment with K_2CO_3 gave the *anti*-tetrahydroquinolones **37** and **38** in good yield. The relative stereochemistry of **37** and **38** was confirmed by X-ray crystallography.[5b] The cleavage reaction was next investigated in the model system. Treatment of **37** and **38** with SmI_2 using LiCl as a promotor[18] gave the expected products in moderate, unoptimized yields. The use of LiCl as a promotor, rather than DMPU, simplifies the purification procedure even further. Further modification of **37** was readily achieved by alkylation to give **41**, the relative stereochemistry of which was confirmed by X-ray crystallography.[5b] Cleavage using SmI_2/LiCl gave **42** as a ∼1:1 mixture of diastereoisomers. Interestingly, the use of *t*-BuOH as a proton source in the reduction gave *syn*-**42** as the major product (5:1 dr) (Scheme 3). The relative stereochemistry of the major diastereoisomer was confirmed by X-ray crystallography.[5b]

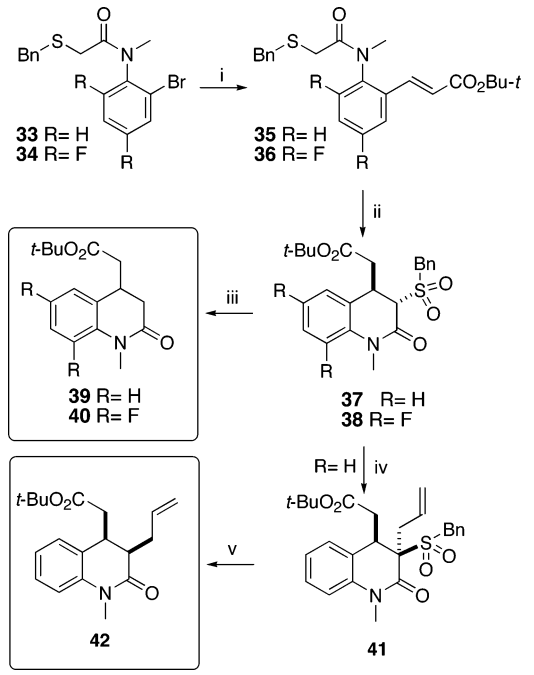
Satisfied that our approach was feasible we moved on to the solid phase. An early reaction sequence on resin is shown in Scheme 7.

Immobilization of α-bromoamide **43** gave amide **44**. Microwave-assisted Heck reaction with *tert*-butyl acrylate was unsatisfactory using *o*-xylene because of poor swelling of the resin and because it gave low conversion as indicated by FTIR. The use of a DMF/*o*-xylene solvent mixture in the Heck reaction appeared to solve this issue and gave **45**. Cyclization then gave supported tetrahydroquinolone **46**. As expected, treatment of **46** with SmI_2/LiCl gave **39** although in a disappointing overall yield of 15% (for 5 steps). The isolation of amide byproducts **47** and **48** indicated that the Heck reaction was not proceeding efficiently on the solid phase. The debrominated product **48** most likely results from SmI_2 reduction during the cleavage step although it is possible that reduction of the aryl bromide occurs under the conditions of the Heck reaction. Although *o*-xylene was an excellent solvent for the Heck reaction in solution, it was clearly unsuitable for use on solid phase. The use of JandaGel, a support more suitable for use with nonpolar solvents such as *o*-xylene, also gave **39** in low yield. A more detailed solution phase study on the pivotal Heck reaction was therefore carried out to provide improved conditions for use on solid phase (Table 1). The use of a combination of DMF and *o*-xylene (3:7) gave lower conversion (entry 3). In neat DMF, a more suitable

(17) For an example, see Arnold, L. A.; Luo, W.; Guy, R. K. *Org. Lett.* **2004**, *6*, 3005.

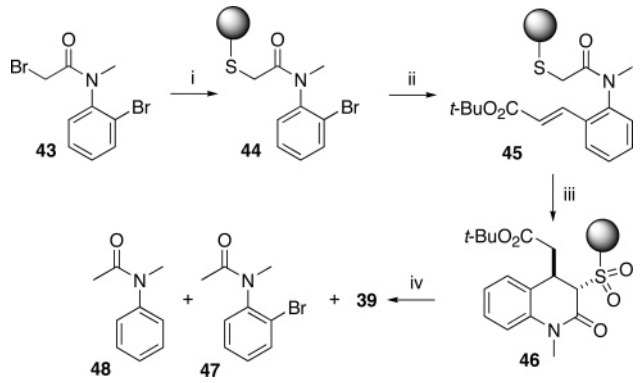
(18) (a) Fuchs, J. R.; Mitchell, M. L.; Shabangi, M.; Flowers, R. A. II *Tetrahedron Lett.* **1997**, *38*, 8157. (b) Miller, R. S.; Sealy, J. M.; Shabangi, M.; Kuhlman, M. L.; Fuchs, J. R.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2000**, *122*, 7718. (c) Hughes, A. D.; Price, D. A.; Simpkins, N. S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1295.

SCHEME 6[a]



[a] Reagents and conditions: (i) *tert*-butyl acrylate, $Pd(OAc)_2$ (5 mol %), $P(o\text{-Tol})_3$ (5 mol %), NEt_3 *o*-xylene, MW 100 °C, 7 h, 88% **35**, 99% **36**. (ii) 1. Oxone, DMF/H_2O (4:1), rt. 2. K_2CO_3, DMF, for two steps 99% **37**, 92% **38**. (iii) SmI_2, THF, LiCl, rt, unoptimized, 57% **39**, 45% **40**. (iv) K_2CO_3, allyl bromide, DMF, rt, 76%. (v) SmI_2, THF, LiCl, *t*-BuOH, rt, 79% (5:1, syn/anti).

SCHEME 7[a]

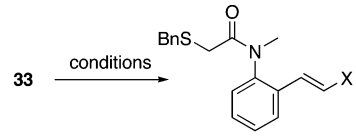


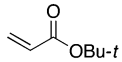
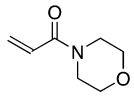
[a] Reagents and conditions: (i) **2**, NEt_3, DMF, rt. (ii) *tert*-butyl acrylate, $Pd(OAc)_2$ (10 mol %), $P(o\text{-Tol})_3$ (10 mol %), NEt_3, DMF−*o*-xylene, MW 100 °C. (iii) 1. Oxone, DMF/H_2O, rt. 2. K_2CO_3, DMF, rt. (iv) SmI_2, THF, LiCl, rt, 15% overall **39**.

solvent for solid phase reactions, conversion was acceptable particularly after a retreatment (entries 4 and 5).

The improved Heck coupling conditions were applied in the solid-phase sequence previously described with the additional modification that *m*-CPBA was used for oxidation to the sulfone. (The use of oxone for the oxidation caused problems with inorganic byproducts contaminating the resin after washing. Solution phase oxidation of sulfide **35** with *m*-CPBA gave the corresponding sulfone in 71% yield (*m*-CPBA, K_2CO_3, CH_2Cl_2, 2 h, rt). Longer reaction times led to some epoxidation of the electron-deficient alkene). Pleasingly, employing these conditions gave **39** in an improved 27% overall yield after purification (Figure 5). We have utilized the approach to prepare a collection of tetrahydroquinolones using α-bromoamide starting

TABLE 1. Optimizing the Heck Reaction



entry		conditions[a]	hours	yield[b]
1		*o*-xylene, thermal	48	39%
2	"	*o*-xylene, MW	7	88%
3	"	DMF–*o*-xylene (3:7), MW	10 x 2	75%
4	"	DMF, MW 100 °C	10 x 2	90%
5		DMF, MW 100 °C	10 x 2	76%

[a] $Pd(OAc)_2$ (5 mol %), $P(o\text{-Tol})_3$ (5 mol %), NEt_3. [b] Isolated yields.

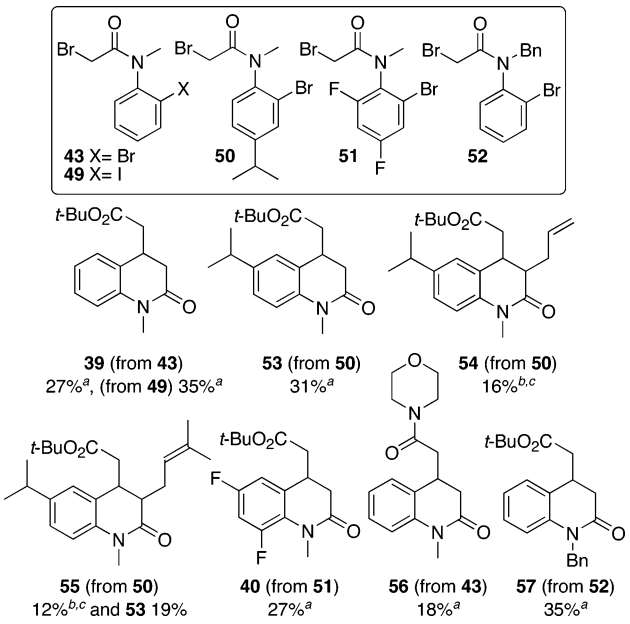
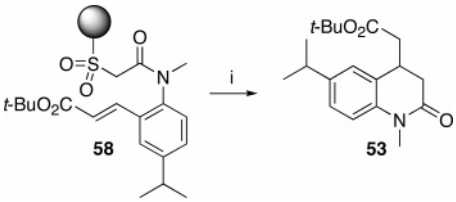


FIGURE 5. Starting materials and tetrahydroquinolone products for (*a*) 5 and (*b*) 6 steps and (*c*) 2:1 to 1:1 diastereoisomeric ratio.

materials **43**, **49**−**52**. Additional diversity was introduced by Heck reaction with a different olefin and by the alkylation of an intermediate sulfone.

The expected products were obtained in satisfactory overall yields in five and six steps on solid phase. Aryl iodide **49** gave improved yields owing to more efficient Heck reactions. Alkylations of intermediate sulfones proved to be more difficult than solution models had predicted and more forcing conditions were necessary (50 °C, KI). Products **54** and **55** were obtained with little diastereoselectivity possibly because of residual moisture in the resin acting as an alternative proton source to the added *t*-BuOH. Finally, we have investigated the feasibility of a cyclative cleavage strategy using the HASC linker. Pleasingly, treatment of sulfone **58** with SmI_2 resulted in cleavage of the sulfur linkage and cyclization to give **53** in good overall yield. The cyclization may be either a radical or anionic process (Scheme 8).

SCHEME 8[a]



[a] Reagents and conditions: (i) SmI_2, THF, LiCl, rt, 25% for four steps.

Conclusions

We have developed a solid-phase approach to *N*-heterocycles using a sulfur linker cleaved using SmI_2. The route to oxindoles employs the first Pummerer cyclizations on solid phase, while the route to tetrahydroquinolones involves a microwave-assisted Heck reaction followed by a Michael cyclization. In both cases, the linker is cleaved in a traceless fashion by reduction with samarium(II) iodide. We have also shown the feasibility of cyclative-cleavage processes using the linker. The routes illustrate the compatibility of the linker system with a number of important reaction types and its utility for library synthesis.

Experimental Section

Preparation of SmI_2. Samarium (II) iodide was prepared by the method of Imamoto[19] with the modification that the samarium−iodine solution was heated at 60 °C rather than at reflux.

General Washing and Drying Procedure. The resin was washed with THF (30 mL), THF/H_2O (3:1) (3 × 30 mL), THF/H_2O (1:1) (3 × 30 mL), THF/H_2O (1:3) (3 × 30 mL), THF (2 × 30 mL), then alternate washings with CH_2Cl_2 (3 × 30 mL) and MeOH (3 × 30 mL), finishing with THF (2 × 30 mL). The resin was then left to dry for 10 min under water pump pressure before being dried for approximately 6 h under high vacuum.

(i) Thioacetate Route to Thiol Resin 2. Merrifield Thioacetate Resin[10].

Merrifield resin (5.00 g, 6.00 mmol) was swollen in DMF (50 mL) for 15 min. Potassium thioacetate (1.88 g, 16.5 mmol) in DMF (10 mL) was added, and the reaction mixture was stirred slowly at room temperature for 24 h before washing according to the standard procedure. υ_{max} (ATR)/cm^{-1}: 2917, 2023, 1687 (C═O), 1493, 1450, 1130.

Thiol Resin 2[10]. Thioacetate resin (5.15 g, 6.13 mmol) was swollen in THF for 15 min. $LiBH_4$ (0.66 g, 30.6 mmol) was added, and the reaction mixture was stirred slowly at room temperature for 48 h. The reaction was then quenched by dropwise addition of MeOH, and the resin **2** was washed according to the standard procedure. υ_{max} (ATR)/cm^{-1}: 3024, 2918, 1601, 1493, 1450, 1065. Loading was determined using the procedure outlined in the general methods section.

(i) Thiourea Route to Thiol Resin 2. *S*-Merrifield Bound Isothiouronium Chloride. Merrifield resin (1.00 g, 1.1 mmol/g, 1.1 mmol, 1 equiv) was swollen in DMF (10 mL) for 15 min. Thiourea (419 mg, 5.5 mmol, 5 equiv) was added, and the reaction was heated at 60 °C for 24 h. The resin was then washed using the standard washing protocol. The product resin was then dried in vacuo. υ_{max} (ATR)/cm^{-1}: 1648 (C═N).

Benzyl Thiol Resin 2[10]. *S*-Merrifield bound isothiouronium chloride (1.07 g, 1.02 mmol/g, 1.09 mmol, 1 equiv) was swollen in DMF (10 mL). *n*-Butylamine (0.28 mL, 5.45 mmol, 5 equiv) was added, and the reaction was heated at 60 °C for 18 h. The resin was then washed using our standard washing protocol. Thiol resin **2** was then dried in vacuo. IR analysis showed disappearance of the C═N stretch. υ_{max} (ATR)/cm^{-1}: 3024, 2918, 1601, 1493, 1450, 1065. Loading was determined using the procedure outlined in the general methods section.

***N*-Benzyl-2-bromo-*N*-(3-methoxy-phenyl) Acetamide 3.** To a solution of *N*-benzyl-3-methoxyaniline (878 mg, 4.12 mmol, 1 equiv) and NEt_3 (0.87 mL, 6.20 mmol, 1.5 equiv) in CH_2Cl_2 (30 mL) at 0 °C was added bromoacetyl bromide (0.54 mL, 6.20 mmol, 1.5 equiv). The reaction was allowed to stir at room temperature for 7 h. The reaction mixture was then washed with 0.5 M HCl (3 × 20 mL) and aqueous saturated NaCl (3 × 20 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo to give *N*-benzyl-2-bromo-*N*-(3-methoxy-phenyl) acetamide **3** (1.34 g, 4.09 mmol, 99%) as a brown oil which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.64 (2H, s, CH_2-CO), 3.65 (3H, s, CH_3O), 4.81 (2H, s, PhCH_2), 6.49 (1H, apparent triplet, J = 2.1 Hz, Ar*H*), 6.57 (1H, d, J = 7.8 Hz, Ar*H*), 6.81 (1H, dd, J = 8.3, 2.2 Hz, Ar*H*), 7.12−7.23 (6H, m, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.7 (*C*H_2CO), 54.0 (Ph*C*H_2), 55.7 (*C*H_3O), 114.1 (Ar*C*H), 114.8 (Ar*C*H), 120.6 (Ar*C*H), 128.1 (Ar*C*H), 128.8 (2 × Ar*C*H), 129.3 (2 × Ar*C*H), 130.8 (Ar*C*H), 137.1 (Ar*C*), 142.6 (Ar*C*), 160.7 (Ar*C*O), 166.8 (*C*═O). υ_{max} (neat)/cm^{-1}: 3029, 1662 (C═O), 1600, 148, 1286. *m*/*z* (EI$^+$ mode): 333 (M$^+$, 5%), 254 (82), 212 (12), 150 (80), 91 (100), 65 (12). $C_{16}H_{16}NO_2Br$ requires 333.0364; found, 333.0361.

***N*-Benzyl-2-benzylsulfanyl-*N*-(3-methoxy-phenyl)-acetamide 4.** To a solution of *N*-benzyl-2-bromo-*N*-(3-methoxyphenyl) acetamide **3** (300 mg, 0.90 mmol, 1 equiv) in DMF (4 mL) was added NEt_3 (0.13 mL, 0.90 mmol, 1 equiv) and benzyl thiol **2** (0.11 mL, 0.90 mmol, 1 equiv). The reaction was allowed to stir at room temperature for 4.5 h. CH_2Cl_2 (10 mL) was added, and the organic layer was washed with water (3 × 10 mL) and aqueous saturated $NaHCO_3$ (3 × 10 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (30% ethyl acetate in petroleum ether as eluant) to give *N*-benzyl-2-benzyl sulfanyl-*N*-(3-methoxyphenyl)-acetamide **4** (160 mg, 0.44 mmol, 49%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.86 (2H, s, CH_2CO), 3.60 (3H, s, CH_3O), 3.82 (2H, s, PhCH_2S), 4.80 (2H, s, PhCH_2), 6.43 (1H, d, J = 2.3 Hz, Ar*H*), 6.49 (1H, d, J = 7.8 Hz, Ar*H*), 6.73 (1H, dd, J = 8.3, 2.3 Hz, Ar*H*), 7.09−7.25 (11H, m, 11 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.5 (*C*H_2), 36.7 (*C*H_2), 53.5 (Ph*C*H_2), 55.7 (*C*H_3O), 114.4 (Ar*C*H), 120.9 (Ar*C*H), 127.4 (Ar*C*H), 127.8 (Ar*C*H), 128.8 (4 × Ar*C*H), 129.1 (2 × Ar*C*H), 129.6 (2 × Ar*C*H), 130.5 (Ar*C*H), 137.7 (Ar*C*), 138.1 (Ar*C*), 143.3 (Ar*C*), 160.6 (Ar*C*O), 169.7 (*C*═O). υ_{max} (neat)/cm^{-1}: 3060, 3027, 2937, 1650 (C═O), 1600, 1488, 1390. *m*/*z* (EI$^+$ mode): 377 (M$^+$, 8%), 255 (62), 213 (16), 164 (5), 122 (10), 91 (100), 65 (10). $C_{23}H_{23}NO_2S$ requires 377.1449; found, 377.1451.

(±)-*N*-Benzyl-2-benzylsulfinyl-*N*-(3-methoxyphenyl) Acetamide 5. To a solution of *N*-benzyl-2-benzylsulfanyl-*N*-(3-methoxyphenyl) acetamide **4** (126 mg, 0.34 mmol, 1 equiv) in HFIP/CH_2Cl_2 (4 mL: 2 mL) was added 30% aqueous H_2O_2 (0.15 mL, 1.36 mmol, 4 equiv), and the reaction was allowed to stir at room temperature for 1 h. The reaction was then quenched with aqueous saturated Na_2SO_3 solution. The aqueous and organic layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give (±)-*N*-benzyl-2-benzylsulfinyl-*N*-(3-methoxyphenyl) acetamide **5** as a yellow oil (122 mg, 0.31 mmol, 92%) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.26 (1H, d, AB system, J = 14.6 Hz, 1H from PhCH_2S), 3.35 (1H, d, AB system, J = 14.6 Hz, 1H from PhCH_2S), 3.59 (3H, s, OCH_3), 4.05 (1H, d, AB system, J = 13.0 Hz, 1H from CH_2CO), 4.24 (1H, d, AB system, 13.0 Hz, 1H from CH_2CO), 4.75 (1H, d, AB system, J = 14.2 Hz, 1H from PhCH_2N), 4.85 (1H, d, AB system, J = 14.2 Hz, 1H from PhCH_2N), 6.33 (1H, apparent triplet, J = 2.2 Hz, Ar*H*), 6.43 (1H, dd, J = 7.8, 1.0 Hz, ArH), 6.73−6.76 (1H, multiplet, Ar*H*), 7.08 − 7.30 (11H, m, 11 × ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0 (PhCH_2S), 52.7 (*C*H_2CO), 54.4 (O*C*H_3), 56.4 (Ph*C*H_2N), 112.9 (Ar*C*H), 113.5 (Ar*C*H), 119.3 (Ar*C*H), 126.7

(19) Imamoto, T.; Ono, M. *Chem. Lett.* **1987**, 501.

(Ar*C*H), 127.3 (Ar*C*H), 127.5 (2 × Ar*C*H), 127.7 (2 × Ar*C*H), 127.9 (2 × Ar*C*H), 128.5 (Ar*C*), 129.5 (3 × Ar*C*H), 135.5 (Ar*C*), 140.8 (Ar*C*), 159.5 (Ar*C*O), 163.4 (C=O). υ_{max} (neat)/cm^{-1}: 3060, 3029, 2919, 1644 (C=O), 1587, 1488, 1402, 1164. *m*/*z* (EI$^+$ mode): 393 (M$^+$, 10%), 255 (16), 212 (6), 91 (100), 83 (24), 65 (7). $C_{23}H_{23}NO_3S$ requires 393.1399; found, 393.1400.

(±)-1-Benzyl-3-benzylsulfanyl-6-methoxy-1,3-dihydro-indol-2-one 6. To a solution of (±)-*N*-benzyl-2-benzylsulfinyl-*N*-(3-methoxyphenyl) acetamide **5** (41.2 mg, 0.11 mmol, 1 equiv) in 1,2-dichloroethane (4 mL) was added TFAA (93 μL, 0.66 mL, 6 equiv), and the reaction was allowed to stir at room temperature for 2 h. The reaction was quenched with 5% NaOH solution (5 mL), and the aqueous and organic layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (20% ethyl acetate in petroleum ether) to give (±)-1-benzyl-3-benzylsulfanyl-6-methoxy-1,3-dihydro-indol-2-one **6** (26 mg, 0.07 mmol, 63%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.64 (3H, s, C*H*$_3$O), 3.68−3.72 (1H, m, 1H from PhC*H*$_2$), 4.04−4.16 (2H, m, 1H from PhC*H*$_2$ and C*H*S), 4.75 (2H, s, PhC*H*$_2$N), 6.19 (1H, d, *J* = 2.2 Hz, Ar*H*), 6.42 (1H, dd, *J* = 2.2, 8.2 Hz, Ar*H*), 7.08 (1H, d, *J* = 8.2 Hz, Ar*H*), 7.14−7.32 (10H, m, 10 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.7 (Ph*C*H$_2$S), 43.2 (*C*HS), 44.3 (Ph*C*H$_2$N), 55.8 (*C*H$_3$O), 97.7 (Ar*C*H), 106.9 (Ar*C*H), 117.5 (Ar*C*), 126.2 (Ar*C*H), 127.6 (Ar*C*H), 127.7 (2 × Ar*C*H), 128.1 (Ar*C*H), 128.7 (2 × Ar*C*H), 129.2 (2 × Ar*C*H), 129.7 (2 × Ar*C*H), 136.0 (Ar*C*), 137.8 (Ar*C*), 144.9 (Ar*C*), 161.0 (Ar*C*O), 176.8 (*C*=O). υ_{max} (neat)/cm^{-1}: 2915, 2838, 1720 (C=O), 1621, 1496, 1373, 1164. *m*/*z* (EI$^+$ mode): 375 (M$^+$, 5%), 253 (100), 252 (82), 162 (5), 91 (85), 65 (7). $C_{23}H_{21}NO_2S$ requires 375.1293; found, 375.1292.

Solution Phase Model Cleavage of (±)-1-Benzyl-3-benzylsulfanyl-6-methoxy-1,3-dihydro-indol-2-one 6. To a solution of (±)-1-benzyl-3-benzylsulfanyl-6-methoxy-1,3-dihydro-indol-2-one **6** (19 mg, 0.05 mmol, 1 equiv) in THF (2 mL) and DMPU (0.05 mL) was added SmI_2 (0.15 mL of a 1 M solution in THF, 0.15 mmol, 3 equiv) at room temperature, and the reaction was stirred for 18 h. The reaction mixture was then diluted with CH_2Cl_2 (4 mL) and the organic layer washed with aqueous saturated $NaHCO_3$ (2 mL) before being dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (40% ethyl acetate in petroleum ether) to give 1-benzyl-6-methoxy-1,3-dihydro-indol-2-one **7**−*major* (6 mg, 0.025 mmol, 48%) as a colorless oil.

2-Bromo-*N*-methyl-*N*-phenylacetamide 8[20]. To a solution of *N*-methyl aniline (0.33 mL, 3.00 mmol, 1 equiv) and NEt_3 (0.42 mL, 3.00 mmol, 1 equiv) in CH_2Cl_2 (3.5 mL) at 0 °C was added by cannula, a solution of bromoacetyl bromide (0.26 mL, 3.00 mmol, 1 equiv) in CH_2Cl_2 (5 mL). The reaction was allowed to stir at room temperature for 16 h. CH_2Cl_2 (10 mL) was then added to the reaction, the organic layer was washed with 0.5 M HCl (3 × 20 mL) and aqueous saturated NaCl (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo, to give 2-bromo-*N*-methyl-*N*-phenylacetamide **8** (0.60 g, 2.63 mmol, 88%) as a brown solid which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (3H, s, NC*H*$_3$), 3.65 (2H, s, C*H*$_2$Br), 7.22 (2H, d, *J* = 7.3 Hz, 2 × Ar*H*) and 7.31−7.41 (3H, m, 3 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.2 (*C*H$_2$Br), 38.5 (N*C*H$_3$), 127.4 (2 × Ar*C*H), 128.9 (Ar*C*H), 130.4 (2 × Ar*C*H), 143.5 (Ar*C*) and 166.9 (*C*=O). υ_{max} (neat)/cm^{-1}: 3060, 2969, 1662 (C=O), 1594, 1496, 1382, 1226, 1118 and 701 (C−Br). *m*/*z* (FAB mode): 228 ((M + H)$^+$, 100%), 227 (20), 199 (5), 148 (17), 106 (11), 92 (3) and 69 (3). $C_9H_{11}NOBr$ requires 228.0024; found, 228.0023.

2-Bromo-*N*,*N*-diphenylacetamide 13[21]. To a solution of *N*,*N*-diphenylamine (0.68 g, 4.00 mmol, 1 equiv) and NEt_3 (0.56 mL, 4.00 mmol, 1 equiv) in CH_2Cl_2 (10 mL) at 0 °C was added by cannula, a solution of bromoacetyl bromide (1.05 mL, 12.0 mmol, 3.0 equiv) in CH_2Cl_2 (5 mL), and the reaction was allowed to stir at room temperature for 16 h. CH_2Cl_2 (10 mL) was added to the reaction, and the organic layer was washed with 0.5 M HCl (3 × 20 mL) and brine (3 × 20 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by recrystallization from petroleum ether/methanol to give 2-bromo-*N*,*N*-diphenylacetamide **13** (0.49 g, 1.68 mmol, 42%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.87 (2H, s, C*H*$_2$CO), 7.18−7.59 (10H, broad signal, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.3 (*C*H$_2$Br), 125−131 (10 × Ar*C*H). *m*/*z* (EI$^+$ mode): 289 (M+, 32%), 222 (4), 196 (14)), 169 (100), 167 (53), 86 (30), 84 (48), 49 (25). $C_{14}H_{12}BrNO$ requires 289.0102; found, 289.0103.

2-Bromo-*N*-allyl-*N*-phenylacetamide 14. To a solution of *N*-allylaniline (1.0 g, 7.50 mmol, 1 equiv) and NEt_3 (1.05 mL, 7.50 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at 0 °C was added a solution of bromoacetyl bromide (1.96 mL, 22.5 mmol, 3 equiv) in CH_2Cl_2 (5 mL), and the reaction was allowed to stir at room temperature for 18 h. The reaction mixture was then washed with 0.5 M HCl (3 × 20 mL) and brine (3 × 20 mL). The organic layer was dried ($MgSO_4$), and concentrated in vacuo. The crude reaction was purified by flash chromatography on alumina using 40% ethyl acetate in petroleum ether as eluant to give 2-bromo-*N*-allyl-*N*-phenylacetamide **14** (868 mg, 3.38 mmol, 45%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (2H, s, C*H*$_2$Br), 4.32 (2H, d, *J* = 6.1 Hz, C*H*$_2$N), 5.15 (2H, apparent t, *J* = 7.5 Hz, C*H*$_2$=CH), 5.83−5.93 (1H, m, C*H*=CH$_2$), 7.22−7.28 (2H, m, Ar*H*), 7.39−7.48 (3H, m, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.6 (*C*H$_2$Br), 53.3 (*C*H$_2$N), 119.0 (*C*H$_2$=CH), 128.5 (2 × ArCH), 129.1 (Ar*C*H), 130.2 (2 × Ar*C*H), 132.5 (*C*H=CH$_2$), 141.8 (Ar*C*), 166.5 (*C*=O). υ_{max}(neat)/cm^{-1}: 1666 (C=O), 1594, 1494, 1394, 1276. *m*/*z* (EI$^+$ mode): 253 (M$^+$, 8%), 212 (7), 174 (100), 132 (25), 106 (28), 83 (65), 77 (35), 41 (19). $C_{11}H_{12}BrNO$ requires 253.0102; found, 253.0107.

2-Bromo-*N*-methyl-*N*-(3-methylphenyl)-acetamide 15. To a solution of *N*-methyl toluidine (1.00 mL, 7.80 mmol, 1 equiv) and NEt_3 (1.20 mL, 8.60 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL) at 0 °C was added bromoacetyl bromide (0.74 mL, 8.60 mmol, 1.1 equiv); the reaction was allowed to stir at room temperature for 1.5 h. The reaction mixture was then washed with 0.5 M HCl (3 × 20 mL) and brine (3 × 20 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo to give 2-bromo-*N*-methyl-*N*-(3-methylphenyl) acetamide **15** (660 mg, 2.73 mmol, 35%) as a red/brown solid which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.33 (3H, s, C*H*$_3$−Ar), 3.22 (3H, s, NC*H*$_3$), 3.60 (2H, s, C*H*$_2$Br), 7.00 (2H, overlapping singlet and doublet, 2 × Ar*H*), 7.13 (1H, d, *J* = 8.0 Hz, Ar*H*), 7.25 (1H apparent t, *J* = 7.6 Hz, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7 (*C*H$_3$Ar), 27.3 (*C*H$_2$Br), 38.4 (*C*H$_3$N), 124.3 (Ar*C*H), 127.9 (Ar*C*H), 129.7 (Ar*C*H), 130.1 (Ar*C*H), 140.6 (Ar*C*), 143.4 (Ar*C*), 166.9 (*C*=O). υ_{max}/(cm^{-1}): 3045, 2962, 1664 (C=O), 1376, 1114. *m*/*z* (EI$^+$ mode): 241 (M$^+$, 7%), 162 (9), 121 (13), 83 (100), 47 (17). $C_{10}H_{12}BrNO$ requires 241.0102; found, 241.0104.

***N*-Benzo[1,3]dioxol-5-yl-2-bromo-*N*-(3-cyclopentyl-propyl)-acetamide 16.** To a solution of 3,4-(methylenedioxy) aniline (1.72 g, 12.5 mmol, 1 equiv) in CH_2Cl_2 (20 mL) was added NEt_3 (1.94 mL, 13.8 mmol, 1.1 equiv) and 3-cyclopentyl propionyl chloride (1.94 mL, 13.8 mmol, 1.1 equiv). The reaction was allowed to stir at room temperature for 3 h before EtOAc was added to the reaction mixture. After separation, the organic layer was washed with $NaHCO_3$, dried ($MgSO_4$) and concentrated to give a white solid. To a solution of the crude amide (3.20 g, 12.2 mmol, 1 equiv) in THF (45 mL) at 0 °C was added $LiAlH_4$ (972 mg, 25.6 mmol, 2.1 equiv). The reaction was allowed to stir at room temperature for 18 h. The reaction was quenched with H_2O. The aqueous and organic layers were separate, and the aqueous layer was washed with $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo. The crude reaction mixture was purified by flash chromatography using 50% petroleum ether in CH_2Cl_2 as eluant to give benzo[1,3]dioxol-5-yl-(3-cyclopentyl-propyl)-amine (1.07 g, 4.38 mmol, 35%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07−1.12 (2H, m, 2H

from 2 × CH_2), 1.37−1.49 (2H, m, CH_2), 1.50−1.67 (6H, m, 3 × CH_2), 1.73−1.87 (3H, m, CH and 2H from 2 × CH_2), 3.07 (2H, t, J = 7.3 Hz, CH_2N), 5.89 (2H, s, CH_2O_2), 6.18 (1H, dd, J = 2.3, 8.3 Hz, Ar*H*), 6.36 (1H, d, J = 2.3 Hz, Ar*H*), 6.69 (1H, d, J = 8.3 Hz, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 (2 × *C*H_2), 28.7 (*C*H_2), 33.1 (2 × *C*H_2), 33.9 (*C*H_2), 40.3 (*C*H), 46.6 (*C*H_2), 97.2 (Ar*C*H), 101.1 (*C*H_2O_2), 106.1 (Ar*C*H), 109.0 (Ar*C*H), 141.0 (Ar*C*O), 143.0 (Ar*C*O), 148.7 (*C*=O). υ_{max}(neat)/cm^{-1}: 3399 (NH), 2857, 1633, 1504, 1199. *m*/*z* (EI$^+$ mode): 247 (M$^+$, 68%), 150 (100), 137 (8), 65(5). $C_{15}H_{21}NO_2$ requires 247.1572; found, 247.1572.

To a solution of benzo[1,3]dioxol-5-yl-(3-cyclopentyl-propyl)-amine (1.07 g, 4.30 mmol, 1 equiv) in CH_2Cl_2 (50 mL) at 0 °C was added NEt_3 (1.20 mL, 8.60 mmol, 2 equiv) and bromoacetyl bromide (0.45 mL, 5.20 mmol, 1.2 equiv), and the reaction was allowed to stir at room temperature for 14 h. The reaction mixture was washed with 0.5 M HCl and $NaHCO_3$, dried ($MgSO_4$), and concentrated to give *N*-benzo[1,3]dioxol-5-yl-2-bromo-*N*-(3-cyclopentyl-propyl) acetamide **16** as a brown oil (1.53 g, 4.13 mmol, 96%) which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97−0.99 (2H, m, 2H from 2 × CH_2), 1.19−1.28 (2H, m, CH_2), 1.35−1.52 (6H, m, 3 × CH_2), 1.62−1.65 (3H, m, CH and 2H from 2 × CH_2), 3.56 (2H, t, J = 7.7 Hz, CH_2N), 3.60 (2H, s, CH_2Br), 5.98 (2H, s, CH_2O_2), 6.65 (2H, m, 2 × Ar*H*), 6.76 (1H, d, J = 8.7 Hz, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 (*C*H_2), 27.0 (*C*H_2), 27.8 (*C*H_2CO), 33.0 (2 × *C*H_2), 33.4 (2 × *C*H_2), 40.3 (*C*H), 50.6 (*C*H_2N), 102.4 (*C*H_2O_2), 209.0 (Ar*C*H), 109.1 (Ar*C*H), 122.0 (Ar*C*H), 135.64 (Ar*C*N), 148.1 (Ar*C*O), 148.9 (Ar*C*O), 166.8 (*C*=O). υ_{max}(neat)/cm^{-1}: 1661 (C=O), 1623, 1504, 1484, 1228. *m*/*z* (EI$^+$ mode): 367 (M$^+$, 57%), 288 (23), 257 (25), 192 (14), 150 (100), 111(29), 69 (30), 41 (15). $C_{17}H_{22}NO_3Br$ requires 367.0783; found, 367.0788.

2-Bromo-*N*-(4-iodophenyl)-*N*-propylacetamide 17. To a solution of 4-iodoaniline 389 (3.00 g, 13.7 mmol, 1 equiv) in CH_2Cl_2 (60 mL) was added NEt_3 (5.78 mL, 41.1 mmol, 3 equiv) and propionic anhydride (3.51 mL, 27.4 mmol, 3 equiv). The reaction was allowed to stir at room temperature for 3 h. The reaction mixture was washed with $NaHCO_3$ and 1 M HCl, dried ($MgSO_4$), and concentrated in vacuo to give a white solid. THF (100 mL) was added the solution cooled to 0 °C. $LiAlH_4$ (1.09 g, 28.8 mmol, 2.1 equiv) was added slowly. The reaction was allowed to stir at room temperature for 18 h. The reaction was quenched with H_2O. The aqueous and organic layers were separated, and the aqueous layer was washed with $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo to give a yellow oil. The crude reaction mixture was purified by flash chromatography using 50% petroleum ether in CH_2Cl_2 as eluant to give 4-iodo-*N*-propyl aniline (1.31 g, 4.93 mmol, 36%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (3H, t, J = 7.4 Hz, CH_3), 1.60−1.69 (2H, m, CH_2CH$_3$), 3.07 (2H, t, J = 7.1 Hz, CH_2N), 3.75 (1H, broad s, N*H*), 6.34−6.40 (2H, apparent dt, J = 3.0, 9.8 Hz, 2 × Ar*H*), 7.41−7.45 (2H, apparent dt, J = 3.0, 9.8 Hz, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.9 (*C*H$_3$), 22.9 (*C*H_2), 46.1 (CH$_2$N), 77.9 (Ar*C*I), 115.3 (2 × Ar*C*H), 138.1 (2 × Ar*C*H), 148.3 (Ar*C*). υ_{max}(neat)/cm^{-1}: 2962, 1604, 1506, 1321. *m*/*z* (EI$^+$ mode): 261 (M$^+$, 62%), 232 (92), 105 (36), 84 (100), 47 (17). $C_9H_{12}NI$ requires 261.0015; found, 261.0014.

To a solution of 4-iodo-*N*-propyl aniline (813 mg, 3.11 mmol, 1 equiv) and NEt_3 (0.87 mL, 6.22 mmol, 2 equiv) in CH_2Cl_2 (20 mL) at 0 °C was added bromoacetyl bromide (0.35 mL, 4.04 mmol, 1.3 equiv) and the reaction was allowed to stir at room temperature for 1.5 h. The reaction mixture was then washed with 0.5 M HCl (3 × 20 mL) and brine (3 × 20 mL). The organic layer was then dried ($MgSO_4$) and concentrated in vacuo to give 2-bromo-*N*-(4-iodophenyl)-*N*-propylacetamide **17** (1.02 g, 2.67 mmol, 86%) as a brown oil which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (3H, t, J = 7.2 Hz, CH_3), 1.41−1.51 (2H, m, CH_2), 3.53 (2H, s, CH_2CO), 3.57 (2H, t, J = 7.6 Hz, CH_2N), 6.95 (2H, apparent d, J = 8.4 Hz, 2 × Ar*H*), 7.71 (2H, apparent d, J = 8.4 Hz, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.2 (*C*H$_3$), 20.7 (*C*H_2), 27.2 (*C*H_2), 51.5 (*C*H_2N), 94.1 (Ar*C*I), 130.1 (2 × Ar*C*H), 139.5 (2 × Ar*C*H), 141.3 (Ar*C*), 165.7 (*C*=O). υ_{max}(neat)/cm^{-1}: 2961, 2930, 1655 (C=O), 1481, 1211. *m*/*z* (CI$^+$ mode): 384 ((M+H)$^+$, 43%), 382 ((M+H)$^+$, 43%), 302 (45), 256 (40), 218 (27), 176 (100), 136 (20). $C_{11}H_{14}NOBrI$ requires 381.9304; found, 381.9305.

2-Bromo-*N*-(4-chlorophenyl)-*N*-propylacetamide 18. To a solution of 4-chloroaniline (1.18 g, 14.2 mmol, 1 equiv) in CH_2Cl_2 (40 mL) was added NEt_3 (4.00 mL, 28.4 mmol, 2 equiv) and propionic anhydride (2.00 mL, 15.6 mmol, 1.1 equiv). The reaction was allowed to stir at room temperature for 3 h. The reaction mixture was washed with $NaHCO_3$ and 1 M HCl, dried ($MgSO_4$), filtered, and concentrated in vacuo to give a white solid. THF (100 mL) was added, and the solution was cooled to 0 °C before the addition of $LiAlH_4$ (1.02 g, 26.8 mmol, 2 equiv). The reaction was then allowed to stir at room temperature for 18 h before being quenched with H_2O. The aqueous and organic layers were separated, and the aqueous layer was washed with $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo to give 4-chloro-*N*-propyl aniline (2.12 g, 24.9 mmol, 93%) as a yellow oil which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (3H, t, J = 7.4 Hz, CH_3CH$_2$), 1.62−1.72 (2H, m, CH_2), 3.08 (2H, t, J = 7.1 Hz, CH_2N), 3.67 (1H, broad singlet, N*H*), 6.55 (2H, apparent doublet, J = 8.8 Hz, 2 × Ar*H*), 7.14 (2H, apparent doublet, J = 8.9 Hz, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.01 (*C*H$_3$), 23.0 (*C*H_2), 46.3 (*C*H_2N), 114.1 (2 × Ar*C*H), 121.9 (Ar*C*Cl), 129.6 (2 × Ar*C*H), 147.5 (Ar*C*N). υ_{max}(neat)/cm^{-1}: 3413 (NH), 1598, 1496, 1317, 1176. *m*/*z* (EI$^+$ mode): 169 (M$^+$, 70%), 143 (25), 140 (100), 111 (26), 82 (45), 77 (14), 46 (7). $C_9H_{12}NCl$ requires 169.0658; found, 169.0657.

To a solution of *N*-propyl-4-chloroaniline (1.18 g, 10.7 mmol, 1 equiv) and NEt_3 (4.5 mL, 32.1 mmol, 3 equiv) in CH_2Cl_2 (40 mL) at 0 °C was added bromoacetyl bromide (1.23 mL, 13.9 mmol, 1.3 equiv) and the reaction allowed to stir at room temperature for 16 h. The reaction mixture was washed with 0.5 M HCl and 1 M NaOH. The organic layer was dried ($MgSO_4$) and concentrated in vacuo to give 2-bromo-*N*-(4-chlorophenyl)-*N*-propylacetamide **18** (3.11 g, 10.7 mmol, 100%) as a brown oil which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (3H, t, J = 7.4 Hz, CH_3), 1.36−1.51 (2H, m, CH_2), 3.51−3.61 (4H, m, CH_2N and CH_2CO), 7.16 (2H, apparent d, J = 8.7 Hz, 2 × Ar*H*), 7.39 (2H, apparent d, J = 8.7 Hz, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.5 (*C*H$_3$), 21.1 (*C*H_2), 27.4 (*C*H_2CO), 51.9 (*C*H_2N), 129.8 (2 × Ar*C*H), 130.9 (2 × Ar*C*H), 134.9 (Ar*C*), 140.4 (Ar*C*), 166.6 (*C*=O). υ_{max}(neat)/cm^{-1}: 2962, 2931, 1658 (C=O), 1488. *m*/*z* (EI$^+$ mode): 289 (M$^+$, 7%), 249 (11), 140 (52), 84 (100), 47 (15). $C_{11}H_{13}NOClBr$ requires 288.9869; found, 288.9875.

General Procedure A: The Immobilization of α-Bromo Acetamides Using 2. *S*-Merrifield Bound *N*-Benzyl-2-mercapto-*N*-(3-methoxyphenyl) Acetamide. Benzyl thiol resin **2** (617 mg, 0.56 mmol/g, 0.35 mmol, 1 equiv) was swollen in DMF (5 mL) for 15 min, and NEt_3 (0.22 mL, 1.56 mmol, 4.6 equiv) was added. A solution of *N*-benzyl-2-bromo-*N*-(3-methoxyphenyl) acetamide **3** (520 mg, 1.56 mmol, 4.6 equiv) in DMF (3 mL) was then added by cannula. The reaction was allowed to stir at room temperature for 18 h. The resin was then washed using our standard washing protocol. The product resin was then dried in vacuo. υ_{max} (ATR)/cm^{-1}: 1650 (C=O).

***S*-Merrifield Bound 2-Mercapto-*N*-methyl-*N*-(3-methylphenyl)acetamide.** As for general procedure A. Thiol resin **2**, on treatment with 2-bromo-*N*-methyl-*N*-(3-methylphenyl) acetamide **15** gave *S*-Merrifield bound 2-mercapto-*N*-methyl-*N*-(3-methylphenyl)acetamide. υ_{max} (ATR)/cm^{-1}: 1650 (C=O).

***S*-Merrifield Bound 2-Mercapto-*N*,*N*-diphenylacetamide.** As for general procedure A. Thiol resin 2, on treatment with 2-bromo-*N*,*N*-diphenyl acetamide 13 gave *S*-Merrifield bound 2-mercapto-*N*,*N*-diphenylacetamide. υ_{max} (ATR)/cm^{-1}: 1664 (C=O).

***S*-Merrifield Bound 2-Mercapto-*N*-methyl-*N*-phenylacetamide.** As for general procedure A. Thiol resin **2**, on treatment with 2-bromo-*N*-methyl-*N*-phenyl acetamide **8** gave *S*-Merrifield bound 2-mercapto-*N*-methyl-*N*-phenylacetamide. υ_{max} (ATR)/cm^{-1}: 1654 (C═O).

***S*-Merrifield Bound *N*-Allyl-2-mercapto-*N*-phenylacetamide.** As for general procedure A. Thiol resin **2**, on treatment with 2-bromo-*N*-allyl-*N*-phenyl acetamide **14** gave *S*-Merrifield bound *N*-allyl-2-mercapto-*N*-phenylacetamide. υ_{max} (ATR)/cm^{-1}: 1652 (C═O).

***S*-Merrifield Bound *N*-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(3-cyclopentylpropyl)-2- mercaptoacetamide.** As for general procedure A. Thiol resin **2**, on treatment with *N*-benzo[1,3]dioxol-5-yl-2-bromo-*N*-(3-cyclopentyl-propyl) acetamide **16** gave *S*-Merrifield bound *N*-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(3-cyclopentylpropyl)-2-mercaptoacetamide. υ_{max} (ATR)/cm^{-1}: 1650 (C═O).

***S*-Merrifield Bound *N*-(4-chlorophenyl)-2-mercapto-*N*-propylacetamide.** As for general procedure A. Thiol resin **2**, on treatment with 2-bromo-*N*-(4-chlorophenyl)-*N*-propylacetamide **18** gave product resin *S*-Merrifield bound *N*-(4-chlorophenyl)-2-mercapto-*N*-propylacetamide. υ_{max} (ATR)/cm^{-1}: 1652 (C═O).

***S*-Merrifield Bound *N*-(4-iodophenyl)-2-mercapto-*N*-propylacetamide.** As for general procedure A. Thiol resin **2**, on treatment with 2-bromo-*N*-(4-iodophenyl)-*N*-propylacetamide **17** gave *S*-Merrifield bound *N*-(4-iodophenyl)-2-mercapto-*N*-propylacetamide. υ_{max} (ATR)/cm^{-1}: 1650 (C═O).

General Procedure B: Oxidation of Resin Bound Sulfides to Sulfoxides. *S*-Merrifield Bound *N*-Benzyl-*N*-(3-methoxyphenyl)-2-sulfinyl Acetamide. *S*-Merrifield bound *N*-benzyl-2-mercapto-*N*-(3-methoxyphenyl) acetamide **(**716 mg, 0.49 mmol/g, 0.35 mmol, 1 equiv) was swollen in HFIP (4 mL) and CH_2Cl_2 (2 mL). An amount of 30% aqueous H_2O_2 (0.26 mL, 2.28 mmol, 6.5 equiv) was then added, and the reaction was allowed to stir at room temperature overnight. The resin was then washed using the standard washing protocol. The product resin was then dried in vacuo. υ_{max} (ATR)/cm^{-1}: 1670 (C═O).

***S*-Merrifield Bound *N*-Methyl-*N*-(3-methylphenyl)-2-(sulfinyl) Acetamide.** As for general procedure B. Upon oxidation, *S*-Merrifield bound 2-mercapto-*N*-methyl-*N*-(3-methylphenyl)acetamide gave *S*-Merrifield bound *N*-methyl-*N*-(3-methylphenyl)-2-(sulfinyl) acetamide. υ_{max} (ATR)/cm^{-1}: 1650 (C═O).

***S*-Merrifield *N*,*N*-Diphenyl-2-(sulfinyl) Acetamide.** As for general procedure B. Upon oxidation, *S*-Merrifield bound 2-mercapto-*N*,*N*-diphenylacetamide gave product resin *S*-Merrifield *N*,*N*-diphenyl-2-(sulfinyl) acetamide. υ_{max} (ATR)/cm^{-1}: 1660 (C═O).

***S*-Merrifield Bound *N*-Methyl-*N*-phenyl-2-(sulfinyl) Acetamide.** As for general procedure B. Upon oxidation, *S*-Merrifield bound 2-mercapto-*N*-methyl-*N*-phenylacetamide gave *S*-Merrifield bound *N*-methyl-*N*-phenyl 2-(sulfinyl) acetamide. υ_{max} (ATR)/cm^{-1}: 1650 (C═O).

***S*-Merrifield Bound *N*-Allyl-*N*-phenyl-2-sulfinyl Acetamide.** As for general procedure B. Upon oxidation, *S*-Merrifield bound *N*-allyl-2-mercapto-*N*-phenylacetamide gave *S*-Merrifield bound *N*-allyl-*N*-phenyl-2-sulfinyl acetamide. υ_{max} (ATR)/cm^{-1}: 1648 (C═O).

***S*-Merrifield Bound *N*-(Benzo[*d*][1,3]dioxol-5-yl)-*N*-(3-cyclopentylpropyl)-2-sulfinyl Acetamide.** As for general procedure B. Upon oxidation, *S*-Merrifield bound *N*-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(3-cyclopentylpropyl)-2-mercaptoacetamide gave *S*-Merrifield bound *N*-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(3-cyclopentylpropyl)-2-sulfinyl acetamide. υ_{max} (ATR)/cm^{-1}: 1648 (C═O).

***S*-Merrifield Bound *N*-(4-chlorophenyl)-*N*-propyl-2-sulfinyl Acetamide.** As for general procedure B. Upon oxidation, *S*-Merrifield bound *N*-(4-chlorophenyl)-2-mercapto-*N*-propylacetamide gave *S*-Merrifield bound *N*-(4-chlorophenyl)-*N*-propyl-2-sulfinyl acetamide. υ_{max} (ATR)/cm^{-1}: 1644 (C═O).

***S*-Merrifield Bound *N*-(4-Iodophenyl)-*N*-propyl-2-sulfinyl Acetamide.** As for general procedure B. Upon oxidation, *S*-Merrifield bound *N*-(4-iodophenyl)-2-mercapto-*N*-propylacetamide gave *S*-Merrifield bound *N*-(4-iodophenyl)-*N*-propyl-2-sulfinyl acetamide. υ_{max} (ATR)/cm^{-1}: 1648 (C═O).

General procedure C: Pummerer Cyclization of Electron Rich Aromatic Systems

***S*-Merrifield Bound 1-Benzyl-3-mercapto-6-methoxy-1,3-dihydro-indol-2-one 25−*major* and *S*-Merrifield Bound 1-Benzyl-3-mercapto-4-methoxy-1,3-dihydro-indol-2-one 25−*minor*.** *S*-Merrifield bound *N*-benzyl-*N*-(3-methoxyphenyl)-2-sulfinyl acetamide (671 mg, 0.49 mmol/g, 0.33 mmol, 1 equiv) was swollen in 1,2-dichloroethane (6 mL) for 15 min. Trifluoroacetic anhydride (0.75 mL, 5.3 mmol, 16 equiv) was then added, and the reaction was allowed to stir at room temperature for 18 h. The resin was then washed using the standard washing protocol. The product resin **25** was then dried in vacuo. υ_{max} (ATR)/cm^{-1}: 1714 (C═O).

***S*-Merrifield Bound 5-(3-Cyclopentylpropyl)-7-mercapto-5H-[1,3]dioxolo[4,5-f]indol-6(7H)-one.** As for general procedure C. Upon cyclization, *S*-Merrifield bound *N*-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(3-cyclopentylpropyl)-2-sulfinyl acetamide gave *S*-Merrifield bound 5-(3-cyclopentylpropyl)-7-mercapto-5H-[1,3]dioxolo[4,5-f]-indol-6(7H)-one. ν_{max} (ATR)/cm^{-1}: 1710 (C═O).

General Procedure D: Pummerer Cyclization of Neutral and Electron Deficient Aromatic Systems.

***S*-Merrifield Bound 3-Mercapto-1,6-dimethyl-1,3-dihydro-indol-2-one and *S*-Merrifield Bound 3-Mercapto-1,4-dimethyl-1,3-dihydro-indol-2-one.** *S*-Merrifield bound *N*-methyl-*N*-(3-methylphenyl)-2-(sulfinyl) acetamide and *S*-Merrifield bound *N*-methyl-*N*-(5-methylphenyl)-2-(sulfinyl) acetamide (647 mg, 0.55 mmol/g, 0.36 mmol, 1 equiv) were swollen in 1,2-dichloroethane (6 mL) for 15 min. Trifluoroacetic anhydride (0.85 mL, 0.60 mmol, 17 equiv) was added, and the reaction was allowed to stir at room temperature for 3 h. BF_3·OEt_2 (1.14 mL, 9 mmol, 25 equiv) was added, and the reaction was allowed to stir at room temperature for a further 18 h. The resin was then washed using the standard washing protocol. The product resin was then dried in vacuo. υ_{max} (ATR)/cm^{-1}: 1714 (C═O).

***S*-Merrifield Bound 3-Mercapto-1-phenyl-1,3-dihydro-indol-2-one.** As for general procedure D. Upon cyclization, *S*-Merrifield *N*,*N*-diphenyl 2-(sulfinyl) acetamide gave *S*-Merrifield bound 3-mercapto-1-phenyl-1,3-dihydro-indol-2-one. υ_{max} (ATR)/cm^{-1}: 1722 (C═O).

***S*-Merrifield Bound 3-Mercapto-1-methyl-1,2-dihydro-indol-2-one.** As for general procedure D. Upon cyclization, *S*-Merrifield bound *N*-methyl-*N*-phenyl 2-(sulfinyl) acetamide gave *S*-Merrifield bound 3-mercapto-1-methyl-1,2-dihydro-indol-2-one. υ_{max} (ATR)/cm^{-1}: 1716 (C═O).

***S*-Merrifield Bound 1-Allyl-3-mercapto-1,3-dihydro-indol-2-one.** As for general procedure D. Upon cyclization, *S*-Merrifield bound *N*-allyl-*N*-Phenyl-2-sulfinyl acetamide gave product resin *S*-Merrifield bound 1-allyl-3-mercapto-1,3-dihydro-indol-2-one. υ_{max} (ATR)/cm^{-1}: 1714 (C═O).

***S*-Merrifield Bound 5-Chloro-3-mercapto-1-propyl-1,3-dihydro-indol-2-one.** As for general procedure D. Upon cyclization, *S*-Merrifield bound *N*-(4-chlorophenyl)-*N*-propyl-2-sulfinyl acetamide gave *S*-Merrifield bound 5-chloro-3-mercapto-1-propyl-1,3-dihydro-indol-2-one. υ_{max} (ATR)/cm^{-1}: 1716 (C═O).

***S*-Merrifield Bound 5-Iodo-3-mercapto-1-propyl-1,3-dihydro-indol-2-one.** As for general procedure D. Upon cyclization, *S*-Merrifield bound *N*-(4-iodophenyl)-*N*-propyl-2-sulfinyl acetamide gave *S*-Merrifield bound 5-iodo-3-mercapto-1-propyl-1,3-dihydro-indol-2-one. υ_{max} (ATR)/cm^{-1}: 1714 (C═O).

1-Methyl-1,3-dihydro-indole-2-one 12.[22] *S*-Merrifield bound 3-mercapto-1-methyl-1,2-dihydro-indol-2-one (315 mg, 0.52 mmol/g, 0.16 mmol, 1 equiv) was swollen in THF (4 mL) for 15 min.

(20) Diehl, K.; Himbert, G.; Henn, L. *Chem. Ber*. **1986**, *119*, 2430.
(21) Kleiner, T.; Bongardt, F.; Voegtle, F.; Laeubli, M. W.; Dinten, O.; Simon, W. *Chem. Ber*. **1985**, *118*, 1071.
(22) Tamura, Y.; Uneshi, J. I.; Maeda, H.; Choi, H. D.; Ishibashi, H. *Synthesis* **1981**, 534.

DMPU (0.30 mL, 2.48 mmol, 15.5 equiv), and a solution of SmI_2 (6.20 mL, 0.1 M in THF, 0.62 mmol, 3.9 equiv) were added, and the reaction was allowed to stir at room temperature for 18 h. The resin was filtered, and the solution phase was collected and concentrated in vacuo. Filtration through a short plug of silica washing with 50% ethyl acetate in petroleum ether gave 1-methyl-1,3-dihydro-indole-2-one **12** (10 mg, 0.07 mmol, 43%) as a clear oil. (The yield is over four solid-phase steps based on a loading of 0.56 mmol/g for **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.14 (3H, s, NC*H*$_3$), 3.46 (2H, s, C*H*$_2$CO), 6.75 (1H, d, J = 7.8 Hz, Ar*H*), 6.97 (1H, t, J = 7.5 Hz, Ar*H*) and 7.17−7.24 (2H, m, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1 (N*C*H$_3$), 34.7 (*C*H$_2$CO), 107.1 (Ar*C*H), 121.3 (Ar*C*H), 123.3 (Ar*C*H), 123.5 (Ar*C*), 126.9 (Ar*C*H) 144.2 (Ar*C*) and 174.0 (*C*=O). υ_{max}(neat)/cm^{-1}: 3058, 2942, 2919, 1700 (C=O), 1612, 1463, 1348 and 754. *m*/*z* (EI$^+$ mode): 147 (M$^+$, 90%), 132 (10), 118 (100), 104 (7), 91 (20), 85 (24), 82 (38), 78 (16), 57 (12) and 47(11). C_9H_9NO requires 147.0684; found, 147.0684.

1-Phenyl-1,3-dihydro-indol-2-one 19.[22] *S*-Merrifield bound 3-mercapto-1-phenyl-1,3-dihydro-indol-2-one (577 mg, 0.50 mmol/g, 0.29 mmol, 1 equiv) was swollen in THF (6 mL) for 15 min. DMPU (0.51 mL, 4.2 mmol, 8.4 equiv), and a solution of SmI_2 (10.6 mL, 0.1 M in THF, 1.06 mmol, 3.7 equiv) were added, and the reaction was allowed to stir at room temperature for 18 h. The resin was filtered, and the solution phase was collected and concentrated in vacuo. Filtration through a short plug of silica washing with 40% ethyl acetate in petroleum ether gave 1-phenyl-1,3-dihydro-indol-2-one **19** (24 mg, 0.11 mmol, 39%) as a clear oil. (The yield is over four solid-phase steps based on a loading of 0.56 mmol/g for **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.65 (2H, s, C*H*$_2$), 6.71 (1H, d, J = 7.9 Hz, Ar*H*), 7.0 (1H, t, J = 7.3 Hz, Ar*H*), 7.13 (1H, t, J = 7.5 Hz, Ar*H*), 7.24 (1H, d, J = 7.4 Hz, Ar*H*), 7.32−7.36 (3H, m, 3 × Ar*H*), 7.44−7.57 (2H, m, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.5 (*C*H$_2$CO), 109.8 (Ar*C*H), 123.2 (Ar*C*H), 124.7 (Ar*C*), 125.0 (Ar*C*H), 127.0 (2 × Ar*C*H), 128.2 (Ar*C*H), 128.5 (Ar*C*H), 130.1 (2 × Ar*C*H), 134.9 (Ar*C*), 145.6 (Ar*C*), 174.8 (*C*=O). υ_{max} (neat)/cm^{-1}: 3056, 2948, 2919, 1706 (C=O), 1610, 1590, 1500, 1479, 1365. *m*/*z* (EI$^+$ mode): 209 (M$^+$, 50%), 209 (54), 180 (100), 82 (25), 77 (11), 46 (8). $C_{14}H_{11}NO$ requires 209.0841; found, 209.0840.

1-Allyl-1,3-dihydro-indol-2-one 20.[23] *S*-Merrifield bound 1-allyl-3-mercapto-1,3-dihydro-indol-2-one (641 mg, 0.55 mmol/g, 0.35 mmol, 1 equiv) was swollen in THF (6 mL) for 15 min. DMPU (0.57 mL, 4.70 mmol, 13.4 equiv) and a solution of SmI_2 (11.8 mL of 0.1 M solution in THF, 1.18 mmol, 3.4 equiv) were added and the reaction allowed to stir at room temperature for 18 h. The resin was filtered and the solution phase was collected and concentrated. It was then filtered through a short plug of silica washing with 40% ethyl acetate in petroleum ether to give 1-allyl-1,3-dihydro-indol-2-one **20** (18 mg, 0.10 mmol, 30%) as a clear oil. (The yield is over four solid-phase steps based on a loading of 0.61 mmol/g for **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.5 (2H, s, C*H*$_2$CO), 4.27−4.29 (2H, m, C*H*$_2$N), 5.14−5.19 (2H, m, C*H*$_2$=CH), 5.73−5.82 (1H, m, C*H*=CH$_2$), 6.75 (1H, d, J = 7.8 Hz, Ar*H*), 6.96 (1H, t, J = 7.3 Hz, Ar*H*), 7.15−7.19 (2H, m, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.1 (*C*H$_2$CO), 42.7 (*C*H$_2$N), 109.3 (*C*H=CH$_2$), 117.9 (*C*H$_2$=), 122.7 (Ar*C*H), 124.8 (Ar*C*H), 124.9 (Ar*C*), 128.2 (Ar*C*H), 131.8 (Ar*C*H), 144.8 (Ar*C*), 175.2 (*C*=O). υ_{max} (neat)/cm^{-1}: 3054, 2917, 1702 (C=O), 1612, 1486, 1465, 1349, 1197. *m*/*z* (EI$^+$ mode): 173 (M$^+$, 85%), 144 (31), 130 (51), 118 (26), 84 (100), 77 (17), 47 (20). $C_{11}H_{11}NO$ requires 173.0841; found, 173.0841.

1,6-Dimethyl-1,3-dihydro-indol-2-one 21−*major*[24] and 1,4-Dimethyl-1,3-dihydro-indol-2-one 21−*minor*.[24] *S*-Merrifield bound 3-mercapto-1,6-dimethyl-1,3-dihydro-indol-2-one and *S*-Merrifield bound 3-mercapto-1,4-dimethyl-1,3-dihydro-indol-2-one (584 mg, 0.55 mmol/g, 0.32 mmol, 1 equiv) was swollen in THF (7 mL) for 15 min. DMPU (0.51 mL, 4.20 mmol, 13 eq), and a solution of SmI_2 (10.4 mL, 0.1 M in THF, 1.04 mmol, 3.3 equiv) were then added, and the reaction was allowed to stir at room temperature for 18 h. The resin was filtered, and the solution phase was collected and concentrated in vacuo. Filtration through a short plug of silica washing with 30% ethyl acetate in petroleum ether to gave 1,6-dimethyl-1,3-dihydro-indol-2-one **21**−*major* and 1,4-dimethyl-1,3-dihydro-indol-2-one **21**−*minor* (32.4 mg, 0.20 mmol, 63%) as a 2:1 mixture and as a clear oil. (The yield is over four solid-phase steps based on a loading of 0.61 mmol/g for **2**). For **21**−*major* ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (3H, s, C*H*$_3$Ar), 3.11 (3H, s, NC*H*$_3$), 3.40 (2H, s, C*H*$_2$), 6.57 (1H, s, Ar*H*), 6.77 (1H, d, J = 8.2 Hz, Ar*H*), 6.79 (1H, d, J = 8.2 Hz, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.7 (*C*H$_3$Ar), 25.1 (N*C*H$_3$), 34.5 (*C*H$_2$CO), 108.0 (Ar*C*H), 120.4 (Ar*C*), 121.7 (Ar*C*H), 123.0 (Ar*C*H), 136.9 (Ar*C*), 144.3 (Ar*C*), 174.5 (*C*=O). υ_{max} (neat)/cm^{-1}: 3052, 2937, 1695 (C=O), 1619, 1606, 1467, 1097, 948. *m*/*z* (EI$^+$ mode): 161 (M$^+$, 100%), 132 (83), 117 (24), 91 (19), 83 (34), 57 (18), 55 (10). $C_{10}H_{11}NO$ requires 161.0841; found, 161.0840. For **21**−*minor* ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (3H, s, C*H*$_3$Ar), 3.12 (3H, s, NC*H*$_3$), 3.33 (2H, s, C*H*$_2$), 6.57 (1H, d, J = 9.8 Hz, Ar*H*), 7.03 (1H, d, J = 7.5 Hz, Ar*H*), 7.13 (1H, apparent t, J = 7.8 Hz, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.5 (*C*H$_3$Ar), 25.3 (N*C*H$_3$), 33.7 (*C*H$_2$CO), 104.6 (Ar*C*H), 122.2 (Ar*C*), 122.7 (Ar*C*H), 126.8 (Ar*C*H), 133.0 (Ar*C*), 143.9 (Ar*C*), 174.1 (*C*=O).

1-Benzyl-6-methoxy-1,3-dihydro-indol-2-one 7−*major* and 1-Benzyl-4-methoxy-1,3-dihydro-indol-2-one 7−*minor*. *S*-Merrifield bound 1-benzyl-3-mercapto-6-methoxy-1,3-dihydro-indol-2-one **25**−*major* and *S*-Merrifield bound 1-benzyl-3-mercapto-4-methoxy-1,3-dihydro-indol-2-one **25**−*minor* (598 mg, 0.49 mmol/g, 0.29 mmol, 1 equiv) were swollen in THF (5 mL) for 15 min. DMPU (0.58 mL, 4.8 mmol, 16.5 equiv) and a solution of SmI_2 (12.0 mL of 0.1 M, 1.20 mmol, 4.1 equiv) were added, and the reaction was allowed to stir at room temperature for 15 h. The resin was filtered, and the solution phase was collected and concentrated before filtration through a short plug of silica washing with 30% ethyl acetate in petroleum ether to give 1-benzyl-6-methoxy-1,3-dihydro-indol-2-one **7**−*major* and 1-benzyl-4-methoxy-1,3-dihydro-indol-2-one **7**−*minor* (27.7 mg, 0.11 mmol, 38% as a 9:1 mixture of regioisomers) as a clear oil. (The yield is calculated over four solid-phase steps based on a loading of 0.48 mmol/g for **2**). The regioisomers were separated by chromatography using 20% ethyl acetate in petroleum ether as eluant. **7**−*major* was obtained as a white solid and was recrystallized from EtOH to give crystals suitable for X-ray analysis (mp 104 °C). For **7**−*major* ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (2H, s, C*H*$_2$CO), 3.65 (3H, s, C*H*$_3$O), 4.82 (2H, s, PhC*H*$_2$) 6.25 (1H, d, J = 2.3 Hz, Ar*H*), 6.43 (1H, dd, J = 8.2, 2.3 Hz, Ar*H*), 7.05 (1H, d, J = 8.2 Hz, Ar*H*), 7.16−7.26 (5H, m, 5 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.5 (*C*H$_2$-CO) 44.2 (Ph*C*H$_2$), 55.8 (*C*H$_3$O), 97.7 (Ar*C*H), 106.4 (Ar*C*H), 116.8 (Ar*C*), 125.2 (Ar*C*H), 127.8 (2 × Ar*C*H), 128.0 (Ar*C*H), 129.2 (2 × Ar*C*H), 136.2 (Ar*C*), 145.9 (Ar*C*), 160.2 (Ar*C*O), 176.3 (*C*=O). υ_{max} (ATR)/cm^{-1}: 3002, 2937, 1700 (C=O), 1623, 1594,1496. *m*/*z* (EI$^+$ mode): 253 (M$^+$, 97%), 224 (8), 162 (144), 149 (13), 91 (100), 83 (18), 57 (10). $C_{16}H_{15}NO_2$ requires 253.1103; found, 253.1103.

For **7**−*minor* ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.48 (2H, s, C*H*$_2$-CO), 3.78 (3H, s, C*H*$_3$O), 4.82 (2H, s, PhC*H*$_2$), 6.32 (1H, d, J = 7.8 Hz, Ar*H*), 6.51 (1H, d, J = 8.1 Hz, Ar*H*), 7.07 (1H, apparent t, J = 8.1 Hz, Ar*H*), 7.16−7.26 (5H, m, 5 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.9 (*C*H$_2$CO) 44.3 (Ph*C*H$_2$), 55.8 (*C*H$_3$O), 102.9 (Ar*C*H), 105.8 (Ar*C*H), 111.4 (Ar*C*), 127.8 (2 × Ar*C*H), 127.9 (Ar*C*H), 129.1 (2 × Ar*C*H), 129.5 (Ar*C*H) 136.5 (Ar*C*), 145.9 (Ar*C*), 155.8 (Ar*C*O), 175.9 (*C*=O).

5-(3-Cyclopentylpropyl)-5H-[1,3]dioxolo[4,5-f]indol-6(7H)-one 22. *S*-Merrifield bound 5-(3-cyclopentylpropyl)-7-mercapto-

(23) Ishikuru, M.; Terashima, M. *Tetrahedron Lett*. **1992**, *33*, 6849.

(24) (a) Redcastle, G. W.; Palmer, B. D.; Dobrusin, E. M.; Fry, D. W.; Kraker, A. J.; Denny, W. A. *J. Med. Chem*. **1994**, *37*, 2033. (b) Goehring, R. R.; Sachdeva, Y. P.; Pisipati, J. S.; Sleevi, M. C.; Wolfe, J. F. *J. Am. Chem. Soc*. **1985**, *107*, 435.

5H-[1,3]dioxolo[4,5-f]indol-6(7H)-one (620 mg, 0.48 mmol/g, 0.30 mmol, 1 equiv) was swollen in THF (5 mL) for 15 min. DMPU (0.46 mL, 3.8 mmol, 12.7 equiv) and a solution of SmI_2 (9.6 mL, 0.1 M in THF, 0.96 mmol, 3.2 equiv) were added, and the reaction was allowed to stir at room temperature for 18 h. The resin was filtered, and the solution phase was collected and concentrated *in* vacuo. Filtration through a short plug of silica washing with 30% ethyl acetate in petroleum ether to give 5-(3-cyclopentylpropyl)-5H-[1,3]dioxolo[4,5-f]indol-6(7H)-one **22** (31 mg, 0.11 mmol, 36%) as a clear oil. (The yield is over four solid-phase steps based on a loading of 0.56 mmol/g for **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98−1.02 (2H, m, 2H from 2 × CH_2), 1.26−1.32 (2H, m, CH_2), 1.42−1.60 (6H, m, 3 × CH_2), 1.65−1.70 (3H, m, CH and 2H from 2 × CH_2), 3.37 (2H, s, CH_2CO), 3.56 (2H, t, J = 7.5 Hz, CH_2N), 5.86 (2H, s, CH_2O_2), 6.37 (1H, s, Ar*H*), 6.7 (1H, s, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.5 (2 × *C*H_2), 27.1 (*C*H_2), 33.0 (2 × *C*H_2), 33.7 (*C*H_2), 36.5 (*C*H_2CO), 40.2 (*C*H), 40.7 (*C*H_2N), 92.7 (Ar*C*H), 101.4 (*C*H_2O_2), 106.5 (Ar*C*H), 116.5 (Ar*C*), 139.2 (Ar*C*N), 143.2 (Ar*C*O), 147.5 (Ar*C*O), 175.6 (*C*=O). υ_{max} (neat)/cm^{-1}: 1687 (C=O), 1616, 1500, 1473,1328. *m*/*z* (EI$^+$ mode): 287(M$^+$, 100%), 177 (20), 162 (45), 132 (28), 104 (5), 77 (7), 41 (14). $C_{17}H_{21}NO_3$ requires 287.1521; found, 287.1520.

5-Iodo-1-propyl-1,3-dihydro-indol-2-one 23. *S*-Merrifield bound 5-iodo-3-mercapto-1-propyl-1,3-dihydro-indol-2-one (845 mg, 0.48 mmol/g, 0.41 mmol, 1 equiv) was swollen in THF (7 mL) for 15 min. DMPU (0.44 mL, 3.65 mmol, 8.9 equiv) and a solution of SmI_2 (9.10 mL, 0.1 M in THF, 0.91 mmol, 2.2 equiv) were added, and the reaction was allowed to stir at room temperature for 18 h. The resin was filtered, and the solution phase was collected and concentrated in vacuo. Filtration through a short plug of silica washing with 30% ethyl acetate in petroleum ether gave 5-iodo-1-propyl-1,3-dihydro-indol-2-one **23** (24 mg, 0.08 mmol, 20%) as a clear oil. (The yield is over four solid-phase steps based on a loading of 0.56 mmol/g for **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 7.4 Hz, CH_3), 1.56−1.66 (2H, m, CH_2), 3.43 (2H, s, CH_2CO), 3.57 (2H, t, J = 7.3 Hz, CH_2N), 6.44 (1H, d, J = 8.2 Hz, Ar*H*), 7.47 (1H, s, Ar*H*), 7.52 (1H, d, J = 8.2 Hz, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.3 (*C*H_3), 19.6 (*C*H_2), 34.3 (*C*H_2-CO), 40.6 (*C*H_2N), 83.4 (Ar*C*I), 109.3 (Ar*C*H), 126.0 (Ar*C*), 132.2 (Ar*C*H), 135.6 (Ar*C*H), 143.5(Ar*C*), 173.1 (*C*=O). υ_{max} (neat)/cm^{-1}: 2960, 2917, 2848, 1698 (C=O), 1600, 1481. *m*/*z* (EI$^+$ mode): 301 (M$^+$, 100%), 272 (36), 259 (19), 244 (19), 177 (70), 83 (29). $C_{11}H_{12}NOI$ requires 300.9964; found, 300.9964.

5-Chloro-1-propyl-1,3-dihydro-indol-2-one 24.[25] *S*-Merrifield bound 5-chloro-3-mercapto-1-propyl-1,3-dihydro-indol-2-one (0.99 g, 0.50 mmol/g, 0.50 mmol, 1 equiv) was swollen in THF (10 mL) for 15 min. DMPU (0.99 mL, 8.20 mmol, 16.4 equiv) and a solution of SmI_2 (20.5 mL, 0.1 M in THF, 2.05 mmol, 4.1 equiv) were added, and the reaction was allowed to stir at room temperature for 18 h. The resin was filtered, and the solution phase was collected and concentrated in vacuo. Filtration through a short plug of silica washing with 30% ethyl acetate in petroleum ether gave 5-chloro-1-propyl-1,3-dihydro-indol-2-one **24** (39.7 mg, 0.19 mmol, 38%) as a clear oil. (The yield is over four solid phase-steps based on a loading of 0.56 mmol/g for **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (3H, t, J = 7.4 Hz, CH_3), 1.57−1.67 (2H, m, CH_2), 3.45 (2H, s, CH_2CO), 3.59 (2H, t, J = 7.4 Hz, CH_2N), 6.76 (1H, d, J = 7.9 Hz, Ar*H*), 7.15−7.18 (2H, m, 2 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.4 (*C*H_3), 19.7 (*C*H_2), 34.6 (*C*H_2CO), 40.7 (*C*H_2N), 108.1 (Ar*C*H), 123.9 (Ar*C*H), 125.2 (Ar*C*), 126.4 (Ar*C*), 126.7 (Ar*C*H), 142.3 (Ar*C*), 173.4 (C=O). υ_{max} (neat)/cm^{-1}: 1695 (C=O), 1610, 1486, 1342. *m*/*z* (EI+ mode): 209 (M$^+$, 64%), 180 (36), 152 (58), 117 (32), 85 (65), 84 (100), 47 (17). $C_{11}H_{12}NOCl$ requires 209.0607; found, 209.0605.

(25) Wiseman, E. H.; Chiani, J.; McManus, J. M. *J. Med. Chem*. **1973**, *16*, 131.

***S*-Merrifield Bound 1-Benzyl-6-methoxy-3-sulfonyl-1,3-dihydro-indol-2-one 26.** *S*-Merrifield bound 1-benzyl-3-mercapto-6-methoxy-1,3-dihydro-indol-2-one **25** (2.51 g, 0.49 mmol/g, 1.23 mmol, 1 equiv) was swollen in DMF/H_2O (20 mL:5 mL) for 15 min. Oxone (11.4 g, 18.6 mmol, 15.1 equiv) was then added, and the reaction was allowed to stir at room temperature for 18 h. The resin was then washed using the standard washing protocol, and the product resin, *S*- Merrifield bound 1-benzyl-6-methoxy-3-sulfonyl-1,3-dihydro-indol-2-one **26** was then dried in vacuo. υ_{max} (ATR)/cm^{-1}: 1712 (C=O), 1166 (S=O).

***S*-Merrifield Bound 3-Allyl-1-benzyl-6-methoxy-3-sulfonyl-1,3-dihydro-indol-2-one 27.** *S*-Merrifield bound 1-benzyl-6-methoxy-3-sulfonyl-1,2-dihydro-indol-2-one **26** (2.06 g, 0.48 mmol/g, 0.98 mmol, 1 equiv) was swollen in DMF (20 mL) for 15 min. K_2CO_3 (2.56 g, 18.5 mmol, 18.9 equiv), KI (123 mg, 0.74 mmol, 0.76 equiv) and allyl bromide (1.28 mL, 14.8 mmol, 15.1 equiv) were then added, and the reaction was heated at 60 °C for 16 h. The resin was then washed using the standard washing protocol, and the product resin, *S*-Merrifield bound 3-allyl-1-benzyl-6-methoxy-3-sulfonyl-1,3-dihydro-indol-2-one **27**, was then dried in vacuo. υ_{max} (ATR)/cm^{-1}: 1714 (C=O), 1180 (S=O).

3-Allyl-1-benzyl-6-methoxy-1,3-dihydro-indol-2-one 28. *S*-Merrifield bound 3-allyl-1-benzyl-6-methoxy-3-sulfonyl-1,3-dihydro-indol-2-one **27** (1.00 g, 0.47 mmol/g, 0.47 mmol, 1 equiv) was swollen in THF (10 mL) for 15 min. DMPU (1.68 mL, 13.9 mmol, 30 equiv) and a solution of SmI_2 (34.7 mL, 0.1 M in THF, 3.47 mmol, 7.4 equiv) were added, and the reaction was allowed to stir at room temperature for 18 h. The resin was filtered and the solution phase was collected and concentrated in vacuo. Filtration through a short plug of silica washing with 20% ethyl acetate in petroleum ether gave 3-allyl-1-benzyl-6-methoxy-1,3-dihydro-indol-2-one **28** (38.7 mg, 0.13 mmol, 28%) as a clear oil. (The yield is over six solid phase-steps based on a loading of 0.56 mmol/g for **2**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.48−2.56 (1H, m, 1H from CH_2CH=CH_2), 2.71−2.81 (1H, m, 1H from CH_2CH=CH_2), 3.47 (1H, t, J = 6.1 Hz, C*H*), 3.65 (3H, s, CH_3O), 4.72 (1H, d, J = 15.6 Hz, 1H from CH_2N), 4.88 (1H, d, J = 15.6 Hz, 1H from CH_2N), 4.98 (1H, d, J = 10.1 Hz, 1H from CH_2=CH), 5.05 (1H, dd, J = 17.0 Hz, 1.1 Hz, 1H from CH_2=CH), 5.62−5.72 (1H, m, C*H*=CH_2), 6.22 (1H, d, J = 2.2 Hz, Ar*H*), 6.44 (1H, dd, J = 8.1, 2.2 Hz, Ar*H*), 7.10 (1H, d, J = 8.1 Hz, *Ar*H), 7.16−7.27 (5H, m, 5 × Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.3 (*C*H_2CH=CH_2), 43.8 (NCH_2Ph), 44.7 (*C*H), 55.4 (*C*H_3O), 97.2 (Ar*C*H), 105.9 (Ar*C*H), 118.1 (*C*H_2=CH), 120.5 (Ar*C*), 124.7 (Ar*C*H), 127.3 (2 × Ar*C*H), 127.6 (Ar*C*H), 128.6 (2 × Ar*C*H), 134.1 (*C*H=CH_2), 135.9 (Ar*C*), 144.7 (Ar*C*), 159.9 (Ar*C*), 178.0 (C=O). υ_{max} (neat)/cm^{-1}: 1710 (C=O), 1624, 1503, 1382, 1165. *m*/*z* (EI$^+$ mode): 293 (M$^+$, 28%), 252 (100), 91 (75), 83 (39), 47 (8). $C_{19}H_{19}NO_2$ requires 293.1416; found, 293.1415.

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Supporting Information Available: General methods, further experimental, selected IR and MAS ^{1}H NMR and ^{1}H NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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