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Iron-Assisted Nucleophilic Aromatic Substitution on Solid Phase

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Received March 15, 2002

Iron-assisted S_NAr reactions were performed for the first time on solid phase, and a library of 36 unsymmetrically substituted phenylpiperazines and phenyl-1,4-diazepanes was synthesized with this novel strategy. The scope of iron-assisted S_NAr reactions on solid phase was investigated, and reactions of representative nucleophiles from groups VI (O, S, and Se) and V (N and P) of the periodic table were examined. Decomplexation of resin-bound iron complexes was achieved with 1,10-phenanthroline under irradiation, thereby overcoming the notorious disadvantages of decomplexation observed in solution-phase chemistry.

Introduction

During the past decade, combinatorial chemistry and parallel synthesis have been developed to the point where they are now areas of high importance for medicinal and bioorganic chemistry.[1] Prerequisite for the synthesis of combinatorial libraries of highly diverse non-peptide compounds was the development of a large and sophisticated repertoire of reaction types on solid phase.[2]

Iron-activated[3] as well as ruthenium-activated[4] nucleophilic aromatic substitutions (S_NAr) have been systematically and intensively studied in solution. Applications of these metal-assisted S_NAr reactions have been found in a diverse range of areas, including the synthesis of monomers for liquid crystal polymers,[5] macrocylic ethers,[6] unsymmetrical diaryl ethers,[7] novel *p*-phenylendiamines,[8] and biologically active heterocycles,[9] as well as in the α-arylation of carbonyl and heterocarbonyl compounds.[10]

Metal-activated S_NAr reactions, in particular iron-mediated S_NAr reactions, are highly attractive. The reaction takes place with a wide range of nucleophiles under mild conditions, and products are generally obtained in high yields. Furthermore, an inert atmosphere is not required, and starting materials are cheap and readily available. The strategy allows replacement of both chlorine atoms in dichloro-substituted [(cyclopentadienyl)-benzene)Fe(II)]$^+$ PF_6^- complexes. However, the synthesis of unsymmetrically substituted benzenes by sequential replacement of the chlorine atoms cannot always be achieved satisfactorily in solution.[11] In contrast to other methods, for example, covalently bound activating groups such as nitro or carbonyl groups, the activating cyclopentadienyl iron moiety is removable either by pyrolytic sublimation[9a,b,10a] or via ligand exchange with, for example, 1,10-phenanthroline under irradiation.[8a] However,

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10.1021/jo025721q CCC: $22.00
Published on Web 06/27/2002

the decomplexation step is certainly this strategy's major Achilles' heel. Pyrolytic sublimation requires high temperature and, in the case of ligand exchange, the iron salts and an excess of ligand have to be separated from the product.[8a]

Our interest was therefore directed to the development of iron-mediated S_NAr reactions on solid phase. The benefits of solid-phase synthesis would overcome the disadvantages of decomplexation in solution, because iron salts and an excess of ligand would be removed easily by simple filtration and washing. Additionally, the high dilution principle of solid-phase synthesis offers the opportunity to perform selective monosubstitution via S_NAr reactions with symmetrical substrates containing two chemically identical nucleophilic or electrophilic centers.

To explore the application of the iron-activated S_NAr reaction on solid phase, we devoted our efforts to the elaboration of a solid-phase protocol for the general synthesis of ortho-, meta-, and para-heteroatom-substituted phenylpiperazines and related compounds. The substituted *N*-phenylpiperazine moiety acts frequently as the key element in a broad range of biologically active compounds, including marketed drugs such as the antihypertensive urapidil and the antidepressant nefazodone.[12]

Numerous synthetic routes toward *N*-phenylpiperazines are described in the literature. Libraries of aryl piperazines have been synthesized on solid phase and by parallel solution phase synthesis applying different strategies.[13] However, these approaches suffer from some major drawbacks. Elevated temperatures are often required for the S_NAr reaction of activated chloro- or fluorobenzenes with substituted piperazines and covalently bound activating groups or their derivatives are often found in the final compounds.[14] Synthesis of *N*-phenylpiperazines via cyclization of anilines with bis(2-chloroethyl)amine[15] or with *N*-substituted iminodiacetic acids[16] are multistep procedures involving harsh reaction conditions, long reaction times, and highly toxic starting materials and are often low yielding. Novel routes to *N*-arylpiperazines include the coupling of piperazines with aryl halogenides under palladium catalysis[17] or with triarylbismuthines in the presence of copper(II) under mild conditions.[18]

In the present paper, we describe the development of iron-activated S_NAr reactions on solid phase. We demonstrate its first application in solid-phase synthesis by the synthesis of a library of ortho-, meta-, and para-heteroatom-substituted *N*-phenylpiperazines and related compounds.

Results and Discussion

The solid-phase synthesis of substituted phenylpiperazines and phenyl-1,4-diazepanes is outlined in Scheme 1. The starting resin is a commercially available Merrifield resin (loading: 1.1 mmol/g). In the first step, the resin-bound benzyl chloride was treated with piperazine **3a** and 1,4-diazepane **3b** in the presence of *N*-methylmorpholine, yielding the resin-bound diamines **4a** and **4b**, respectively.[19] The loading of **4a** and **4b** was determined by elemental analysis for nitrogen (1.01 and 0.84 mmol/g, respectively), corresponding to yields higher than 80%.

In the second step, an aryl C−N bond was formed by nucleophilic aromatic substitution. The resin-bound amines **4a** and **4b** were treated with the symmetrically substituted η^6-dichlorobenzene-η^5-cyclopentadienyliron(II) hexafluorophosphate complexes **2a**−**d**. Due to the high dilution principle of solid-phase synthesis, only one of the two chemically identical chloride atoms in the symmetrical complexes **2a**−**d** was replaced selectively by the free nitrogen of resin-bound amines **4a** and **4b**. Reaction of the resin-bound amine **4a** under mild conditions with each of the iron complexes **2a**−**d** in excess yielded the corresponding resin-bound iron complexes **5a**−**d**. Resin-bound amine **4b** was treated under the same conditions with iron complex **2a** to yield **5e**. The applied iron complexes **2a**−**d** were synthesized with methods analogous to procedures known from the literature (Scheme 2) in moderate yields (20−38%).[11,20]

The thus-obtained resin-bound iron complexes were able to undergo a second S_NAr reaction by replacing the remaining chloride atom with different nucleophiles in the ortho, meta, and para position of the benzene moiety. To explore the scope of the present methodology, a representative selection of nucleophiles from groups VI (O, S, and Se) and V (N and P) of the periodic table was selected.

The reactivity of the intermediate resin-bound iron complexes **5** toward the sodium salts of alcohols, phenols, alkyl mercaptanes, and thiophenols was investigated. The following nucleophiles were selected as representatives: Sodium 3-methoxyphenylmethoxide (**6**), sodium 2-methoxyphenolate (**7**), sodium cyclohexyl-1-thiolate (**8**), sodium adamantane-1-thiolate (**9**), and sodium 3-methoxy-benzenethiolate (**10**). The selected nucleophiles were generated by deprotonation of the corresponding alcohol, mercaptane, phenol, or thiophenol with sodium hydride prior to reaction with the resin-bound iron complexes **5**. The S_NAr reactions were performed at 60−70 °C in DMF or THF for 16−48 h (methods A and B, Table 1).

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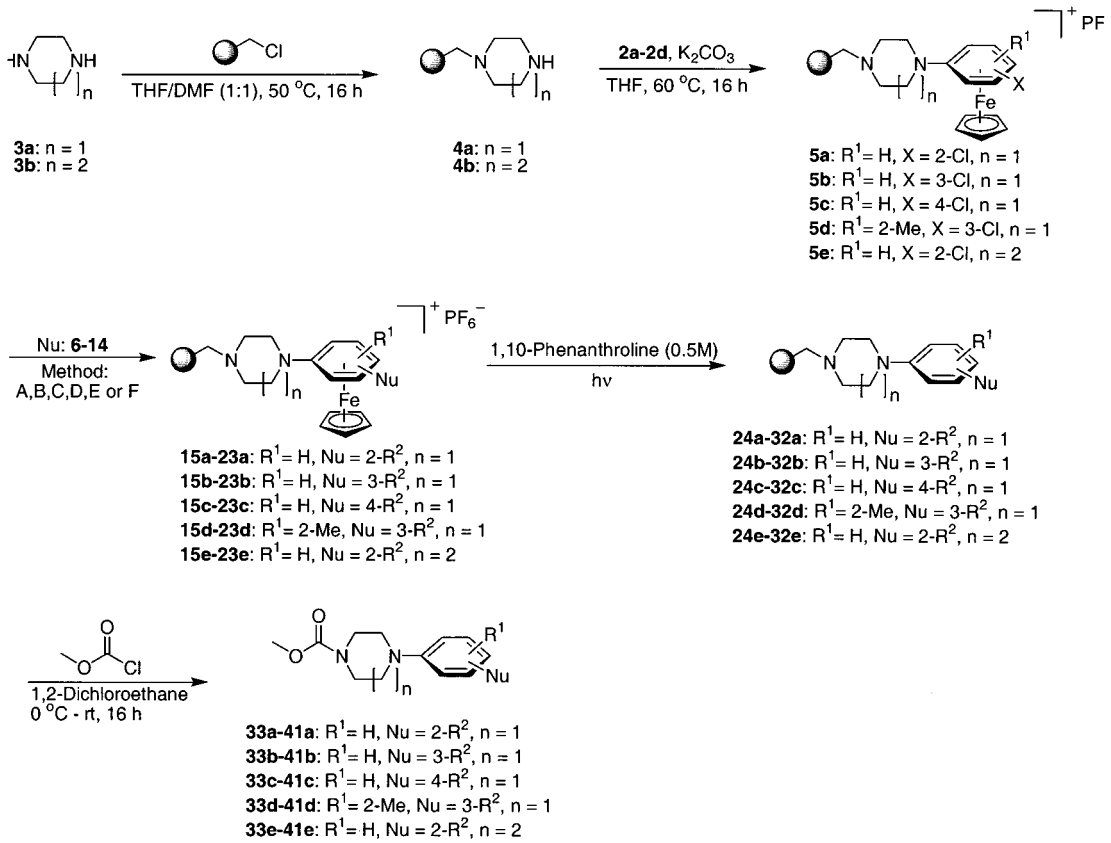
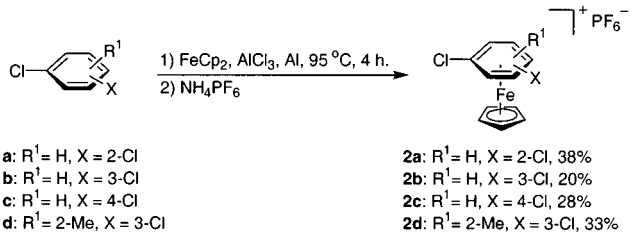
SCHEME 1. Solid-Phase Synthesis of Phenylpiperazines and Phenyl-1,4-diazepanes via the Iron-Assisted S_{NAr} Reaction



SCHEME 2. Preparation of η^6-Dichlorobenzene-η^5-cyclopentadienyliron(II) Hexafluorophosphate Complexes



4-*tert*-Butylphenylselenylmagnesium bromide (**11**) was prepared by addition of elemental selenium to commercially available 4-*tert*-butylphenylmagnesium bromide. The subsequent S_NAr reactions with resin-bound iron complexes **5** were performed at room temperature in a mixture of THF and Et_2O for 48 h (method C, Table 1).

Alkylamines were represented by the secondary and sterically hindered amine, 4-(10,10-dimethyl-9,10-dihydroanthracen-9-yl)piperidine (**12**). The amine was reacted with resins **5** at 90 °C in DMF for 96 h in the presence of an amine base (method D, Table 1).

Commercially available lithium diphenylphosphide **13** was reacted with resin **5a** at 45 °C in THF for 48 h (method E, Table 1) to give resin **22a**. In addition, an unusual Se nucleophile was prepared by the addition of elemental selenium to lithium diphenylphosphide **13**. The generated lithium diphenylphosphinylselenide **14** was reacted with resin **5d** at room temperature in THF for 48 h (method F, Table 1) to give resin **23d**.

The thus-obtained resin-bound iron complexes **15**−**23** were decomplexed prior to cleavage by means of the optimized decomplexation conditions reported by Pearson.[8a] Decomplexation took place by ligand−ligand exchange in the presence of 1,10-phenanthroline under light irradiation (ultraviolet light source, 300 W) to give resins **24**−**32**. Due to the formation of the intensely red-colored phenanthroline iron complex, the progress of the reaction could be monitored easily.

In the final step, the resin-bound phenylpiperazines and phenyl-1,4-diazepanes were cleaved with methyl chloroformate in methylene chloride at room temperature for 16 h[21] to obtain the corresponding carbamates **33**−**41** (Chart 1). The cleavage was followed by a simple aqueous workup that is compatible with automated synthesis of large libraries.

To obtain reliable yields after cleavage, each compound was cleaved from approximately 2.5 g of resins **24**−**32**. Overall yields (four steps) and purities of crude cleavage products are reported in Table 1. The overall yields are based on the loadings of resins **4a** and **4b** determined by elemental analysis, and purities were determined by HPLC [UV detection (254 nm) and evaporative light-scattering detection (ELSD)]. In addition, Table 1 includes the yields of purified products after chromatography.

In general, yields of purified products are as expected based on yields and UV purities of crude products. The

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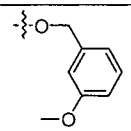
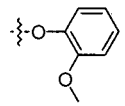
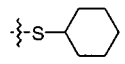
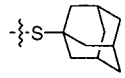
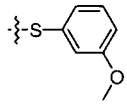
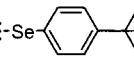
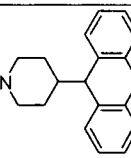
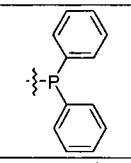
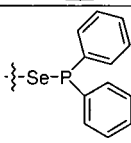
TABLE 1. S_NAr Reactions with Various Nucleophiles[b]

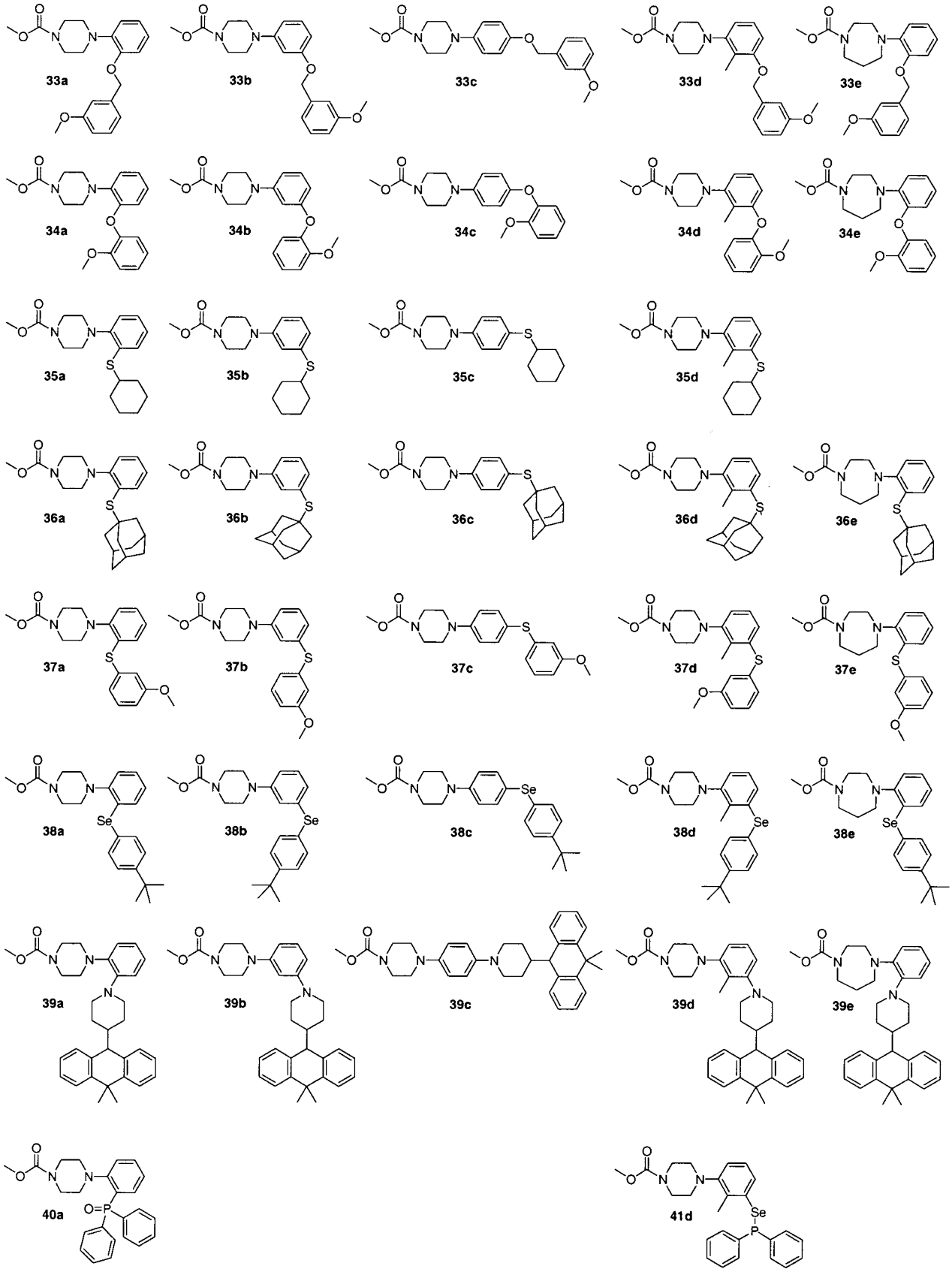
Entry	R^2	Method	Nu	R^1	n	Cleaved product	%UV crude	%ELSD crude	Yield crude	Yield purified
1		A	2-R^2	H	1	**33a**	45	99	80	39
2			3-R^2	H	1	**33b**	45	94	79	35
3			4-R^2	H	1	**33c**	21	93	79	34
4			3-R^2	2-Me	1	**33d**	22	72	67	13
5			2-R^2	H	2	**33e**	28	78	77	23
6		B	2-R^2	H	1	**34a**	93	99	87	63
7			3-R^2	H	1	**34b**	73	97	92	60
8			4-R^2	H	1	**34c**	78	97	84	62
9			3-R^2	2-Me	1	**34d**	80	96	74	51
10			2-R^2	H	2	**34e**	65	94	73	40
11		B	2-R^2	H	1	**35a**	80	92	77	56
12			3-R^2	H	1	**35b**	75	91	86	58
13			4-R^2	H	1	**35c**	83	98	82	56
14			3-R^2	2-Me	1	**35d**	90	98	76	46
15		B	2-R^2	H	1	**36a**	86	98	69	53
16			3-R^2	H	1	**36b**	94	97	86	70
17			4-R^2	H	1	**36c**	89	99	77	54
18			3-R^2	2-Me	1	**36d**	89	99	69	51
19			2-R^2	H	2	**36e**	69	99	64	35
20		B	2-R^2	H	1	**37a**	96	99	97	72
21			3-R^2	H	1	**37b**	95	98	98	71
22			4-R^2	H	1	**37c**	93	99	92	65
23			3-R^2	2-Me	1	**37d**	95	99	93	63
24			2-R^2	H	2	**37e**	92	99	74	50
25		C	2-R^2	H	1	**38a**	75	99	86	70
26			3-R^2	H	1	**38b**	89	85	80	61
27			4-R^2	H	1	**38c**	74	97	87	54
28			3-R^2	2-Me	1	**38d**	80	100	66	45
29			2-R^2	H	2	**38e**	81	100	80	57
30		D	2-R^2	H	1	**39a**	69	90	57	11
31			3-R^2	H	1	**39b**	72	99	84	54
32			4-R^2	H	1	**39c**	78	99	81	53
33			3-R^2	2-Me	1	**39d**	82	98	79	49
34			2-R^2	H	2	**39e**	1	9	42	1
35		E	2-R^2	H	1	**40a**[a]	72	31	80	20
36		F	3-R^2	2-Me	1	**41d**	43	73	70	11

[a] Only the oxidized product was isolated (Chart 1). [b] Method A: R^2Na (**6**) (5 equiv), **5a**−**e** (1 equiv), dry THF, 60 °C, 48 h. Method B: R^2Na (**7**−**10**) (5 equiv), **5a**−**e** (1 equiv), dry DMF, 70 °C, 16 h. Method C: R^2MgBr (**11**) (5 equiv), **5a**−**e** (1 equiv), dry THF, room temperature, 48 h. Method D: R^2H (**12**) (5 equiv), DIEA (6 equiv), **5a**−**e** (1 equiv), dry DMF, 90 °C, 96 h. Method E: R^2Li (**13**) (5 equiv), **5a** (1 equiv), dry THF, 45 °C, 48 h. Method F: R^2Li (**14**), **5d** (1 equiv), dry THF, room temperature, 48 h.

exceptions are yields for compounds for which purification was accomplished with difficulty, thereby resulting in lower recovery of product (see for instance entry 35 in Table 1). The purity based on the ELSD trace seems in general to overestimate the purity of the crude products, indicating that the main impurities are either volatile or possess UV extinction coefficients significantly higher than those of the product. Consequently, the following discussion will be based on yields and UV purities of crude products.

Excellent results were obtained by using the strong nucleophile sodium 3-methoxybenzenethiolate (**10**). The

CHART 1. Product Overview of Synthesized Phenylpiperazines and Phenyl-1,4-diazepanes



3-methoxy-benzenethio-substituted phenylpiperazines **37a**−**d** were isolated in excellent crude yields (>92%) and UV purities (>93%). The overall yields (4 steps) for the crude products **37a**−**d** indicate that each chemical transformation in the reaction sequence proceeded on average with a yield higher than 98%.

The high yields obtained in series **37a**−**e** indicate that the first S_NAr reaction with the iron complex **2a**−**d**, the decomplexation reaction with 1,10-phenanthroline, as well as the cleavage from the solid support all proceed giving excellent yields and purities. These three reactions are common for each compound prepared. Consequently, we can assume that the variations in yields and purities for the final products depend mainly on the nature of the nucleophiles **6**−**13** used in the second S_NAr reaction with the resin-bound iron complexes **15**−**23**.

Some general tendencies of the reactivity between resin-bound iron complexes **5a**−**d** and the nucleophiles have been observed. Within the phenylpiperazine series, none of the substitutions in ortho, meta, or para positions are significantly favored. For example, **37a**, **37b**, and **37c** are obtained in similar yields of 97%, 98%, and 92%, respectively. A possible explanation is that the iron moiety completely changes the electronic nature of the aromatic ring, so that the substitution reaction is no longer governed by the electronic nature of existing substituents to a significant extent (in contrast to substitution of variously substituted fluoronitrobenzenes). The only example in which the ortho position is significantly disfavored is in the case of sterically hindered nucleophiles (**8**, **9**, and **12)**. In the case of **12**, the corresponding ortho-substituted phenylpiperazine **39a** was isolated in 57% yield, whereas the meta- and para-substituted derivatives **39b** and **39c** were isolated in 84% and 81% yields, respectively. Comparison of the reactivity of the two different meta-substituted derivatives **5b** and **5d** indicates that the more restricted meta position in **5b (**having an *o*-methyl substituent) is generally slightly disfavored. For example, **34b** and **34d** are obtained in 92% and 74% yields, respectively. In comparison with ortho-substituted phenylpiperazine derivatives, the analogously substituted phenyl-1,4-diazepane derivatives are obtained in lower yields. For example, **37a** and **37e** are obtained in yields of 97% and 74%, respectively. A possible explanation is that the ortho positions in phenyl-1,4-diazepanes are more sterically hindered than the corresponding phenylpiperazine derivatives.

This explanation is supported by ^{13}C NMR spectra of phenyl-1,4-diazepanes. Compared to ortho-substituted phenylpiperazines, analogously substituted phenyl-1,4-diazepanes often show a set of two carbon signals for carbons in the 1,4-diazepane moiety and in the benzene moiety. This indicates that ortho-substituted phenyl-1,4-diazepanes exist either as distinct rotamers or as ring conformers on the ^{13}C NMR time scale due to hindered rotation around the N−C bond or the presence of the more-flexible seven-membered ring.

Good to excellent overall yields (4 steps) and purities were obtained in the phenylpiperazine series with the remaining strong nucleophiles (phenolates, sulfides, and selenides) **7**, **8**, **9**, and **11** (yields 66−92%; UV purities 74−94%). Even the sterically constrained sodium adamantane-1-thiolate **9** replaced the chlorine atom in the most sterically hindered position (ortho position) in good yields (**36a**, 69% and **36e**, 64%).

All attempts to perform an S_NAr reaction with the strongly nucleophilic phenyltelluride failed. This is in agreement with reports from other authors who have attempted iron-assisted S_NAr reactions with tellurides in solution.[22] Different well-known procedures for the generation of phenyltelluride were tested, such as the reduction of commercially available diphenylditelluride with sodium borohydride, or sodium hydride, as well as the preparation from commercially available phenyllithium and elemental tellurium. With the thus-prepared phenyltellurides present in excess (5 equiv), the S_NAr reaction was carried out in THF or DMF, at both room temperature and 50 °C. After decomplexation and cleavage, only the unsubstituted chlorophenylpiperazines and unidentified side products were obtained. An explanation could be that the phenyltelluride is reoxidized by the iron(II) or undergoes other side reactions with the iron complexes before the nucleophilic attack occurs.

Reactions with Sodium 3-methoxyphenylmethoxide **6** furnished the corresponding 3-methoxybenzyloxy-substituted phenylpiperazines **33a**−**d** and the phenyl-1,4-diazepane **33e** with modest yields (crude: >67%) and UV purities (crude: >21%).

Nitrogen nucleophiles are known as good nucleophiles, well-investigated and high-yielding in iron-assisted S_NAr reactions.[8a] As a representative alkylamine, the sterically hindered amine 4-(10,10-dimethyl-9,10-dihydroanthracen-9-yl)piperidine **12** was chosen. Good yields (>79%) and purities (>72%) were only obtained for the S_NAr attack in the meta and para positions (**5b**, **5c**, and **5d**), resulting in phenylpiperazine derivatives **39b**−**d**. However, the ortho positions in **5a** and especially in **5e** are more sterically hindered and therefore less accessible. This explains the low yields of the ortho-substituted phenylpiperazine **39a** (57%) and especially of the ortho-substituted phenyl-1,4-diazepane **39e** (42%). All attempts to perform an S_NAr reaction with the very weak nucleophile aniline failed. This is in accordance with investigations of Abd-el-Aziz et al. in which aniline replaces only electron-withdrawing leaving groups such as a nitro group, but not a chlorine atom in η^6-aryl-η^5-cyclopentadienyliron(II) complexes.[23]

To further investigate the scope of the described strategy, nucleophiles which have not been applied so far in iron-assisted S_NAr reactions were examined. Phosphorus nucleophiles are known as good nucleophiles and lithium diphenylphosphide **13** has been applied in high-yielding S_NAr reactions in solution.[24] Phosphide **13** was treated under mild conditions (method E, Table 1) with resin-bound complex **5a**. After decomplexation and cleavage, it was found that the phosphorus was oxidized and 2-(diphenylphosphinoyl)phenylpiperazine (**40a**; yield 80%; UV purity 72%) instead of the expected 2-(diphenylphosphinyl)phenylpiperazine (not detected in the crude product either) was isolated. The phosphorus must have been oxidized after nucleophilic attack either by the iron(II) or by photooxidation during decomplexation or by oxygen during workup. The unusual Se nucleophile, lithium diphenylphosphinylselenide **14**, reacted with resin **5d** (method F, Table 1) to give resin **23d**. After decomplexation and cleavage, the 2-[(diphenylphosphinyl)selenyl]-phenylpiperazine derivative **41d** was isolated in good yield (70%) but low UV purity (43%). In contrast to the

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(23) Abd-El-Aziz, A. S.; Piórko, A.; Lee, C. C.; Sutherland, R. G. *Can. J. Chem.* **1989**, *67*, 1618−1624.
(24) (a) Schindlbauer, H. *Monatsh. Chem.* **1965**, *96*, 2051−2057. (b) Sudo, A.; Saigo, K. *J. Org. Chem.* **1997**, *62*, 5508−5513.

phosphorus nucleophile **13,** the phosphorus atom in **14** was not oxidized (oxidation product was not detected in the crude product either). Phenylseleno diphenyl phosphine was first described by McLean,[25] and analogous derivatives have recently found applications as ligands in metal complexes.[26]

There appears to be a distinct trend in the yields obtained for the nucleophiles such as Sodium 2-methoxyphenylmethoxide **6**, sodium 2-methoxyphenolate **7**, sodium cyclohexyl-1-thiolate **8**, and sodium 3-methoxybenzenethiolate **10** in that the yields reflect the relative softness/hardness of the nucleophiles, with the softer nucleophiles giving better yields. Comparisons with the other nucleophiles are more difficult to make (due to differences in counterion and steric bulk), but overall these results suggest that control over the relative hardness of the nucleophiles may lead to better yields. This is plausible, considering the possibly soft nature of the iron complex itself.

Conclusions

We have demonstrated the use of iron-assisted S_NAr reactions on solid phase for the efficient synthesis of a library of unsymmetrically substituted phenylpiperazines and phenyl-1,4-diazepanes. The synthetic strategy demonstrates clearly many important advantages of solid-phase synthesis. Unsymmetrically substituted target molecules are obtained by modular assembly via desymmetrization of commercially or readily available symmetric building blocks in selective and high-yielding transformations. We have demonstrated the scope of S_NAr reactions on solid phase and have applied representative nucleophiles from groups VI (O, S, and Se) and V (N and P) of the periodic table. Only the sodium alkoxides are modest yielding, and anilines and tellurides completely failed. In addition, we demonstrated that all positions (ortho, meta, and para) in the benzene moiety of the iron complexes are almost equally accessible. Resin-bound iron complexes were decomplexed with 1,10-phenanthrolin under irradiation. The notorious disadvantages of decomplexation in solution has been solved since excess of 1,10-phenanthrolin (Phen) and intensively red $[Fe(Phen)_3]^{2+}$ salts are removed from the resin-bound intermediates by a simple washing procedure. Extensions of our strategy, e.g., to resin-bound nucleophiles other than nitrogen, are topics under active investigation in our laboratory.

Experimental Section

All reactions were carried out under nitrogen or argon. Unless otherwise noted, starting materials were from commercial suppliers and were used without further purification. THF was distilled under N_2 from sodium/benzophenone. DMF was dried over molecular sieves (4 Å). Final compounds were purified by flash chromatography. ^{1}H NMR, ^{13}C NMR, ^{31}P, and ^{77}Se spectra were recorded at 500.13, 125.67, 202.45, and 95.36 MHz, respectively. Unless otherwise noted, all compounds were measured in deuterated chloroform. ^{1}H NMR chemical shifts are reported in ppm with TMS as internal reference. ^{13}C NMR chemical shifts are reported in ppm, relative to the chemical shift of $CDCl_3$. ^{13}C NMR chemical shifts in brackets indicate distinct rotamers. Coupling constants (J values) are reported in Hz. The following abbreviations are used for multiplicity of NMR signals: s = singlet, d = doublet, t = triplet, q = quartet, dd = double doublet, and m = multiplet. LC-MS data (Liquid Chromatography Mass Spectroscopy) were obtained on an instrument equipped with a Heated Nebulizer source operating at 425 °C. The LC-MS pumps were running with a symmetry C-18 column (30 mm, 3.5 μm). Solvent A was 100% water + 0.05% trifluoroacetic acid; solvent B was 95% acetonitrile, 5% water + 0.035% trifluoroacetic acid. Gradient (2 mL/min): 10 to 100% B in 4 min, 10% B for 1 min. Total time including equilibration was 5 min (injection volume 10 μL). Purities of compounds were determined by UV detection at 254 nm and by ELSD (Evaporated Light Scattering Detection). Retention times (R_t values) are given in minutes. HRMS (High-Resolution Mass Spectroscopy) was performed at the University of Odense, Department of Chemistry (Odense, Denmark) on a 4.7 T Ultima (IonSpec, Irvine, CA) FTMS (Fourier Transform Mass Spectrometry) with 337 nm MALDI (Matrix Assisted Laser Desorption Ionization). The peak at m/z 273.0393 of $[M - H_2O + H]^+$ ions of the matrix compound (2,5-dihydroxybenzoic acid, DHB) was used for internal calibration. Elemental analyses were performed at the University of Vienna, Department of Physical Chemistry (Vienna, Austria). Melting points were determined uncorrected. For decomplexation by irradiation, an ultraviolet light source (300 W) was used. Chloromethyl polystyrene (Merrifield resin) was purchased (loading: 1.1 mmol/g, 100−200 mesh, cross-linked with 1% divinylbenzene).

Piperazin-1-yl Methyl Polystyrene (4a). Chloromethyl polystyrene (200 g), piperazine (189.5 g, 2.2 mol), and *N*-methylmorpholine (122.4 g, 1.2 mol) were suspended in dry THF/DMF (1:1, 2 L) and stirred overnight at 50 °C. The resin was filtrated off and washed with THF (2 × 250 mL), DMF (2 × 250 mL), MeOH (2 × 250 mL), H_2O (2 × 250 mL), and CH_2Cl_2 (3 × 250 mL) before drying in vacuo at 30 °C. Yield: 208.3 g. Loading of the resin as calculated from the amount of nitrogen found by elemental analysis (Anal. Found: C, 87.40; H, 7.97; N, 2.82): 1.01 mmol/g (theoretical loading: 1.04 mmol/g).

1,4-Diazepan-1-yl Methyl Polystyrene (4b) was prepared according to the procedure described above. Loading of the resin as calculated from the amount of nitrogen found by elemental analysis (Anal. Found: C, 87.94; H, 7.96; N, 2.36): 0.84 mmol/g (theoretical loading: 1.03 mmol/g).

η^6-1,2-Dichlorobenzene-η^5-cyclopentadienyliron(II) Hexafluorophosphate (2a). 1,2-Dichlorobenzene (**1a**) (500 g, 3.4 mol), anhydrous aluminum chloride (91.2 g, 0.68 mol), aluminum powder (9.2 g, 0.34 mol), and ferrocene (63.2 g, 0.34 mol) were heated to 95 °C for 4 h under vigorous stirring. The reaction was cooled to 0 °C, and H_2O (500 mL) was added slowly keeping the temperature below 50 °C. [Caution: Very exothermic!] Et_2O (500 mL) was added, and the reaction mixture was stirred for 30 min. The aqueous phase was isolated, filtrated, and extracted with Et_2O (2 × 200 mL). The dark green aqueous phase was filtered and a saturated aqueous ammonium hexafluorophosphate solution was added in small portions until complete precipitation of the desired product. The precipitate was filtered, washed with H_2O (2 × 200 mL) and Et_2O (2 × 200 mL), and dried in vacuo at 50 °C yielding 53.6 g (38%) of a green crystalline solid. ^{1}H NMR (d_6-DMSO): δ 7.05 (m, 2H), 6.46 (m, 2H), 5.29 (s, 5H). ^{13}C NMR (d_6-DMSO): δ 106.1, 88.3, 87.3, 80.5.

The following Fe complexes (**2b**, **2c**, and **2d**) were prepared analogously:

η^6-1,3-Dichlorobenzene-η^5-cyclopentadienyliron(II) Hexafluorophosphate (2b). Yield: 27.5 g (20%) yellow/green crystals. ^{1}H NMR (d_6-DMSO): δ 7.48 (s, 1H), 6.84 (d, 2H, J = 6.6), 6.62 (t, 1H, J = 6.5), 5.32 (s, 5H). ^{13}C NMR (d_6-DMSO): δ 106.4, 89.0, 87.7, 87.5, 80.9.

η^6-1,4-Dichlorobenzene-η^5-cyclopentadienyliron(II) Hexafluorophosphate (2c). Yield: 38.9 g (28%) yellow/green

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crystals. ^{1}H NMR (d_6-DMSO): δ 6.98 (s, 4H), 5.33 (s, 5H). ^{13}C NMR (d_6-DMSO): δ 105.3, 87.8, 80.5.

η^6-2,6-Dichlorotoluene-η^5-cyclopentadienyliron(II) Hexafluorophosphate (2d). Yield: 43.7 g (33%) green crystals. ^{1}H NMR (d_6-DMSO): δ 6.84 (d, 2H, J = 6.6), 6.54 (t, 1H, J = 6.4), 5.27 (s, 5H), 2.76 (s, 3H). ^{13}C NMR (d_6-DMSO): δ 107.2, 87.7, 86.0, 81.0, 17.4.

{4-[η^6-(2-Chlorophenyl)-η^5-cyclopentadienyliron(II)]-piperazin-1-yl}methyl Polystyrene Hexafluorophosphate (5a). Piperazin-1-yl methyl polystyrene (**4a**) (24 g, 24.2 mmol), η^6-1,2-dichlorobenzene-η^5-cyclopentadienyliron(II) hexafluorophosphate (**2a**) (25 g, 60.6 mmol), and potassium carbonate (13.4 g, 97.0 mmol) were suspended in dry THF (400 mL) and the solution was stirred overnight at 60 °C. The resin was filtered, washed with THF (2 × 100 mL), H_2O (2 × 100 mL), THF (2 × 100 mL), MeOH (2 × 100 mL), and CH_2Cl_2 (3 × 100 mL) and dried in vacuo at 40 °C giving 32.9 g (99%) of **5a** as a red resin.

The resins **5b** (33.4 g, 101%), **5c** (32.8 g, 99%), **5d** (33.0 g, 100%), and **5e** (19.9 g, 101%) were prepared analogously.

Methods for Nucleophilic Aromatic Substitutions. Method A (S_NAr with the sodium salt of alkyl alcohols): A solution of Sodium 3-methoxyphenylmethoxide (**6**, 0.50 M) was prepared by slowly adding 3-methoxyphenylmethanol to sodium hydride (60% suspension in mineral oil) in dry THF at room temperature. [Caution: Generation of heat and hydrogen.] The mixture was stirred for an additional 30 min after gas generation had ceased. The alcoholate (11 mmol) was transferred to resins **5a**, **5b**, **5c**, **5d**, or **5e** (3.0 g, 1.9−2.2 mmol), and THF was added to a total volume of 45 mL. The reactions were stirred at 60 °C for 48 h. The resins were filtered, washed with THF (2 × 50 mL), MeOH (2 × 50 mL), H_2O (2 × 50 mL), MeOH (2 × 50 mL), and CH_2Cl_2 (3 × 50 mL), and dried in vacuo at 40 °C to give resins **15a**−**e**.

Method B (S_NAr with the sodium salt of phenols, thiophenols, and alkylmercaptanes): A solution of sodium 2-methoxyphenolate (**7**, 0.70 M), sodium cyclohexyl-1-thiolate (**8**, 0.25 M), sodium adamantane-1-thiolate (**9**, 0.25 M), and sodium 3-methoxy-benzenephenolate (**10**, 0.50 M) was prepared by adding respectively 2-methoxyphenol, cyclohexanethiol, adamantane-1-thiol, or 3-methoxythiophenyl to sodium hydride (60% suspension in mineral oil) in dry DMF at room temperature. [Caution: Generation of heat and hydrogen.] The mixtures were stirred for an additional 30 min after gas generation had ceased. The alcoholate/thiolate (11 mmol) was transferred to resins **5a**, **5b**, **5c**, **5d**, or **5e** (3.0 g, 1.9−2.2 mmol), and DMF was added to a total volume of 45 mL. The reactions were stirred at 70 °C for 16 h. The resins were filtered, washed with DMF (2 × 50 mL), MeOH (2 × 50 mL), H_2O (2 × 50 mL), MeOH (2 × 50 mL), and CH_2Cl_2 (3 × 50 mL), and dried in vacuo at 40 °C to give resins **16a**−**e**, **17a**−**d**, **18a**−**e,** and **19a**−**e,** respectively.

Method C (S_NAr with the magnesium bromide salt of selenophenols): A solution of 4-*tert*-butylphenylselenylmagnesium bromide (**11**, 0.50 M) was prepared by slowly adding Se powder (7.8 g, 99.8 mmol) to 4-*tert*-butylphenylmagnesium bromide (2.0 M in Et_2O, 50 mL) in dry THF at room temperature. [Caution: Exothermic reation.] The mixture was stirred for an additional 30 min at room temperature after the Se powder had been completely consumed. 4-*tert*-Butylphenylselenylmagnesium bromide (11 mmol) was transferred to resins **5a**, **5b**, **5c**, **5d**, or **5e** (3.0 g, 1.9−2.2 mmol), and the reactions were stirred at room temperature for 48 h. The resins were filtered, washed with DMF (2 × 50 mL), MeOH (2 × 50 mL), H_2O (2 × 50 mL), MeOH (2 × 50 mL), and CH_2Cl_2 (3 × 50 mL), and dried in vacuo at 40 °C to give resin **20a**−**e**.

Method D (S_NAr with alkylamines): Resins **5a**, **5b**, **5c**, **5d**, or **5e** (3 g, 1.9−2.2 mmol), 4-(10,10-dimethyl-9,10-dihydroanthracen-9-yl)piperidine (**12**, 3.2 g, 11 mmol), and diisopropylethylamine (1.7 g, 13.2 mmol) were suspended in dry DMF (40 mL) and stirred at 90 °C for 96 h. The resins were filtered, washed with DMF (2 × 50 mL), MeOH (2 × 50 mL), H_2O (2 × 50 mL), MeOH (2 × 50 mL), and CH_2Cl_2 (3 × 50 mL), and dried in vacuo at 40 °C to give resins **21a**−**e**.

Method E (S_NAr with lithium diphenylphosphide): Lithium diphenylphosphide (**13**, 0.5 M in THF, 30 mL) was added to resin **5a** (3.1 g, 2.3 mmol), and the reaction mixture was stirred at 45 °C for 48 h. The resin was filtered, washed with THF (2 × 50 mL), MeOH (2 × 50 mL), H_2O (2 × 50 mL), MeOH (2 × 50 mL), and CH_2Cl_2 (3 × 50 mL), and dried in vacuo at 40 °C to give resin **22a**.

Method F (S_NAr with lithium diphenylphosphinylselenide): A solution of lithium diphenylphosphinylselenide (**14**, 0.5 M) was prepared by slowly adding Se powder (1.1 g, 14.3 mmol) to lithium diphenylphosphide (**13**, 0.5 M in THF, 30 mL) at room temperature. [Caution: Exothermic reaction.] The mixture was stirred for an additional 30 min at room temperature after the selenium had been completely consumed. Resin **5d** (3.1 g, 2.2 mmol) was added to the selenide, and the reaction mixture was stirred at room temperature for 48 h. The resin was filtered, washed with THF (2 × 50 mL), MeOH (2 × 50 mL), H_2O (2 × 50 mL), MeOH (2 × 50 mL), and CH_2Cl_2 (3 × 50 mL), and dried in vacuo at 40 °C to give resin **23d**.

General Method for Decomplexation of Resin-Bound Iron Complexes. Preparation of 1,10-phenanthroline solution (0.5 M) used for decomplexation: To 1,10-phenanthroline (180.0 g, 1.0 mol) was added under stirring in the following order CH_3CN (600 mL), H_2O (200 mL), concentrated HCl (40 mL), H_2O (160 mL), CH_3CN (900 mL), and finally H_2O (approximately 100 mL) until the solution became clear.

Decomplexation on Solid Phase: The resins **15a**−**e**, **16a**−**e**, **17a**−**d**, **18a**−**e**, **19a**−**e**, **20a**−**e**, **21a**−**e**, **22a**, and **23d** were suspended in a light-transparent reactor tube with the thus prepared 1,10-phenanthroline solution (10 mL/1 g of resin). The suspensions were agitated under irradiation with visible light for 12 h. During this time, the solution became intensely red. The resins were filtered and washed with MeOH (3 × 50 mL), THF (3 × 50 mL), and MeOH (3 × 50 mL) until the washing solution was colorless (approximately 5 cycles). The irradiation procedure was repeated until decomplexation was complete (approximately 5 cycles). After complete decomplexation, the resins were washed with MeOH (3 × 50 mL) and THF (3 × 50 mL) and suspended in a triethylamine solution (1 M in THF) for 1 h. The resins were then further washed with MeOH (3 × 50 mL), CH_2Cl_2 (3 × 50 mL), MeOH (3 × 50 mL,) and CH_2Cl_2 (3 × 50 mL) and dried in vacuo at 50 °C to yield resins **24a**−**e**, **25a**−**e**, **26a**−**d**, **27a**−**e**, **28a**−**e**, **29a**−**e**, **30a**−**e**, **31a**, and **32d**.

Standard Cleavage from Polymer Support: 4-[2-(3-Methoxybenzyloxy)phenyl]piperazine-1-carboxylic Acid Methyl Ester (33a). The procedure for a typical experiment follows. A suspension of resin **24a** (2.41 g, 2.00 mmol) in 1,2-dichloroethane (30 mL) was cooled to 0 °C and neat methyl chloroformate (25.0 mmol) was slowly added. After 1 h of additional stirring at 0 °C, the temperature was raised to room temperature, and the reaction mixture was stirred overnight. The resin was filtered and washed with H_2O (1 × 30 mL), CH_2Cl_2 (1 × 30 mL), and H_2O (1 × 30 mL). The combined filtrates were washed with an aqueous solution of NaOH (1M)-(30 mL), and the two phases separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give 569 mg (80%) of crude **33a** as a dark oil (LC-MS: UV 45%, ELSD 99%, R_t = 2.50). Purification by chromatography [heptane → heptane/EtOAc (75:25)] gave 277 mg (39%) of pale oil (LC-MS: UV 96%, ELSD 99%). ^{1}H NMR: δ 7.29 (t, 1H, J = 8.0), 6.97 (m, 6H), 6.86 (m, 1H), 5.10 (s, 2H), 3.82 (s, 3H), 3.72 (s, 3H), 3.62 (m, 4H), 3.07 (m, 4H). ^{13}C NMR: δ 160.2, 156.4, 151.9, 142.0, 139.2, 130.0, 123.6, 122.1, 119.6, 119.0, 114.0, 113.6, 113.1, 70.8, 55.7, 53.0, 51.0, 44.6. HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_4 + H^+$: m/z

357.1809. Found: *m*/*z* 357.1811. Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.25; H, 6.75; N, 7.83.

4-[3-(3-Methoxybenzyloxy)phenyl]piperazine-1-carboxylic Acid Methyl Ester (33b). This compound was cleaved from resin **24b** (2.40 g, 2.00 mmol) to give 564 mg (79%) of crude **33b** as a dark oil (LC-MS: UV 45%, ELSD 94%, R_t = 2.88). Purification by chromatography [heptane → heptane/EtOAc (75:25)] gave 246 mg (35%) of pale oil (LC-MS: UV 98%, ELSD 99%).^{1}H NMR: δ 7.29 (t, 1H, J = 8.0), 7.17 (t, 1H, J = 8.0), 6.99 (m, 2H), 6.86 (m, 1H), 6.53 (m, 3H), 5.02 (s, 2H), 3.82 (s, 3H), 3.73 (s, 3H), 3.61 (m, 4H), 3.13 (m, 4H). ^{13}C NMR: δ 160.3, 160.2, 156.3, 152.9, 139.1, 130.3, 130.0, 120.1, 113.9, 113.4, 110.0, 106.3, 104.5, 70.3, 55.6, 53.1, 49.6, 44.1. HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_4$: *m*/*z* 356.1731. Found: *m*/*z* 356.1727. Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.29; H, 6.78; N, 7.79.

4-[4-(3-Methoxybenzyloxy)phenyl]piperazine-1-carboxylic Acid Methyl Ester (33c). This compound was cleaved from resin **24c** (2.47 g, 2.05 mmol) to give 577 mg (79%) of crude **33c** as a dark solid (LC-MS: UV 21%, ELSD 93%, R_t = 2.21). Purification by chromatography [heptane → heptan/EtOAc (75:25)] gave 252 mg (34%) of pale solid (LC-MS: UV 95%, ELSD 100%); mp 126−127 °C (Et_2O/heptane). ^{1}H NMR: δ 7.28 (t, 1H, J = 8.0), 6.99 (m, 2H), 6.88 (m, 5H), 5.00 (s, 2H), 3.81 (s, 3H), 3.73 (s, 3H), 3.62 (m, 4H), 3.02 (m, 4H). ^{13}C NMR: δ 160.2, 156.3, 153.9, 146.2, 139.3, 130.0, 120.0, 119.2, 116.0, 113.8, 113.3, 70.8, 55.6, 53.0, 51.2, 44.3. HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_4 + H^+$: *m*/*z* 357.1809. Found: *m*/*z* 357.1814. Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.36; H, 6.82; N, 7.89.

4-[3-(3-Methoxybenzyloxy)-2-methylphenyl]piperazine-1-carboxylic Acid Methyl Ester (33d). This compound was cleaved from resin **24d** (2.47 g, 2.03 mmol) to give 507 mg (67%) of crude **33d** as a dark oil (LC-MS: UV 22%, ELSD 72%, R_t = 3.55). Purification by chromatography [heptane → heptane/EtOAc (75:25)] gave 100 mg (13%) of pale oil (LC-MS: UV 91%, ELSD 98%). ^{1}H NMR: δ 7.28 (t, 1H, J = 8.0), 7.10 (t, 1H, J = 8.0), 7.01 (m, 2H), 6.85 (m, 1H), 6.67 (m, 2H), 5.04 (s, 2H), 3.81 (s, 3H), 3.73 (s, 3H), 3.61 (m, 4H), 2.85 (m, 4H), 2.25 (s, 3H). ^{13}C NMR: δ 160.5, 158.4, 156.7, 153.1, 139.9, 130.2, 127.1, 122.2, 120.0, 113.8, 113.4, 112.7, 108.2, 70.7, 55.9, 53.3, 52.6, 45.0, 11.7. HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_4 + H^+$: *m*/*z* 371.1966. Found: *m*/*z* 371.1961. Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.96; H, 7.00; N, 7.49.

4-[2-(3-Methoxybenzyloxy)phenyl]-[1,4]diazepane-1-carboxylic Acid Methyl Ester (33e). This compound was cleaved from resin **24e** (2.43 g, 1.73 mmol) to give 494 mg (77%) of crude **33e** as a dark oil (LC-MS: UV 28%, ELSD 78%, R_t = 2.02). Purification by chromatography [heptane → heptane/EtOAc (75:25)] gave 144 mg (23%) of pale oil (LC-MS: UV 66%, ELSD 100%). ^{1}H NMR: δ 7.29 (t, 1H, J = 8.0), 7.00 (m, 2H), 6.94 (m, 1H), 6.88 (m, 4H), 5.05 (s, 2H), 3.81 (s, 3H), 3.69 (s, 3H), 3.57 (m, 4H), 3.29 (m, 4H), 1.90 (m, 2H). ^{13}C NMR: δ 160.2, (157.1 + 157.0), 151.7, 143.2, (139.2 + 139.1), 129.9, 122.3, 121.8, (120.4 + 120.3), (119.7 + 119.6), (114.1 + 114.0), (113.9 + 113.6), (112.2 + 112.0), 71.1, 55.6, (54.6 + 54.5), (53.7 + 53.6), (52.9 + 52.8), (48.8 + 48.3), (46.2 + 46.1), 29.1. HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_4 + H^+$: *m*/*z* 371.1966. Found: *m*/*z* 371.1958. Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56. Found: C, 67.81; H, 7.16; N, 7.36.

4-[2-(2-Methoxyphenoxy)phenyl]piperazine-1-carboxylic Acid Methyl Ester (34a). This compound was cleaved from resin **25a** (2.46 g, 2.07 mmol) to give 618 mg (87%) of crude **34a** as a dark oil (LC-MS: UV 93%, ELSD 99%, R_t = 2.88). Purification by chromatography [heptane → heptane/EtOAc (30:10)] gave 449 mg (63%) of pale oil (LC-MS: UV 98%, ELSD 100%). ^{1}H NMR: δ 7.03 (m, 2H), 6.95 (m, 3H), 6.82 (m, 3H), 3.82 (s, 3H), 3.68 (s, 3H), 3.45 (m, 4H), 3.07 (m, 4H). ^{13}C NMR: δ 155.6, 150.2, 149.2, 145.3, 142.3, 123.6, 123.4, 122.8, 120.5, 119.0, 118.9, 118.5, 112.1, 55.5, 52.2, 50.0, 43.7. HRMALDI-FTMS calcd for $C_{19}H_{22}N_2O_4$: *m*/*z* 342.1575. Found: *m*/*z* 342.1577. Anal. Calcd for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18. Found: C, 67.39; H, 6.30; N, 7.86. Contains 3.00% toluene.

4-[3-(2-Methoxyphenoxy)phenyl]piperazine-1-carboxylic Acid Methyl Ester (34b). This compound was cleaved from resin **25b** (2.48 g, 2.09 mmol) to give 657 mg (92%) of crude **34b** as a dark oil (LC-MS: UV 73%, ELSD 97%, R_t = 2.94). Purification by chromatography [heptane → heptane/EtOAc (3:1)] gave 430 mg (60%) of pale oil (LC-MS: UV 100%, ELSD 100%). ^{1}H NMR: δ 7.15 (m, 1H), 7.11 (m, 1H), 6.99 (m, 1H), 6.97 (m, 1H), 6.90 (m, 1H), 6.61 (m, 1H), 6.58 (m, 1H), 6.40 (m, 1H), 3.83 (s, 3H), 3.72 (s, 3H), 3.60 (m, 4H), 3.12 (m, 4H). ^{13}C NMR: δ 158.7, 155.7, 152.4, 151.2, 144.9, 129.7, 124.5, 120.9, 120.8, 112.6, 110.6, 108.6, 105.8, 55.8, 52.5, 48.9, 43.5. HRMALDI-FTMS calcd for $C_{19}H_{22}N_2O_4$: *m*/*z* 342.1575. Found: *m*/*z* 342.1561. Anal. Calcd for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18. Found: C, 66.97; H, 6.53; N, 8.07.

4-[4-(2-Methoxyphenoxy)phenyl]piperazine-1-carboxylic Acid Methyl Ester (34c). This compound was cleaved from resin **25c** (2.51 g, 2.11 mmol) to give 610 mg (84%) of crude **34c** as a dark solid (LC-MS: UV 78%, ELSD 97%, R_t = 2.44). Purification by chromatography [heptane → heptane/EtOAc (30:10)] gave 448 mg (62%) of pale solid (LC-MS: UV 98%, ELSD 100%); mp 117−118 °C (Et_2O/heptane). ^{1}H NMR: δ 7.07 (m, 1H), 6.98 (m, 1H), 6.90 (m, 6H), 3.86 (s, 3H), 3.73 (s, 3H), 3.62 (m, 4H), 3.06 (m, 4H). ^{13}C NMR: δ 156.3, 151.9, 151.3, 147.6, 146.8, 124.3, 121.4, 120.0, 119.3, 118.8, 113.1, 56.4, 53.0, 50.8, 44.3. HRMALDI-FTMS calcd for $C_{19}H_{22}N_2O_4$: *m*/*z* 342.1575. Found: *m*/*z* 342.1588. Anal. Calcd for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18. Found: C, 66.62; H, 6.45; N, 8.17.

4-[3-(2-Methoxyphenoxy)-2-methylphenyl]piperazine-1-carboxylic Acid Methyl Ester (34d). This compound was cleaved from resin **25d** (2.47 g, 2.06 mmol) to give 545 mg (74%) of crude **34d** as a dark solid (LC-MS: UV 80%, ELSD 96%, R_t = 3.28). Purification by chromatography [DCM/EtOAc (20:1) → DCM/EtOAc (10:1)] gave 373 mg (51%) of pale solid (LC-MS: UV 96%, ELSD 98%); mp 82−83 °C (Et_2O/heptane). ^{1}H NMR: δ 7.06 (m, 2H), 6.99 (m, 1H), 6.85 (m, 1H), 6.76 (m, 2H), 6.54 (m, 1H), 3.88 (s, 3H), 3.74 (s, 3H), 3.63 (m, 4H), 2.89 (m, 4H), 2.27 (s, 3H). ^{13}C NMR: δ 156.3, 155.9, 152.6, 150.7, 146.1, 126.4, 123.6, 123.4, 120.9, 119.1, 113.9, 113.1, 112.7, 56.0, 52.5, 51.8, 44.2, 11.0. HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_4 + H^+$: *m*/*z* 357.1809. Found: *m*/*z* 357.1813. Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.47; H, 6.74; N, 7.86.

4-[2-(2-Methoxyphenoxy)-2-phenyl]-[1,4]diazepane-1-carboxylic Acid Methyl Ester (34e). This compound was cleaved from resin **25e** (2.43 g, 1.75 mmol) to give 456 mg (73%) of crude **34e** as a dark oil (LC-MS: UV 65%, ELSD 94%, R_t = 2.31). Purification by chromatography [toluene/EtOAc (30:1)] gave 251 mg (40%) of pale oil (LC-MS: UV 98%, ELSD 100%). ^{1}H NMR: δ 7.01 (m, 4H), 6.83 (m, 3H), 6.75 (m, 1H), 3.86 (s, 3H), 3.66 (m, 3H), 3.56 (m, 1H), 3.49 (m, 2H), 3.38 (m, 3H), 3.31 (m, 2H), 1.86 (m, 2H). ^{13}C NMR: δ (156.7 + 156.6), 150.3, (148.7 + 148.6), (146.1 + 146.0), (144.1 + 143.9), (124.0 + 123.9), (123.5 + 123.4), 121.7, 120.9, (119.9 + 119.8), 119.7, (118.4 + 118.3), 112.5, 55.9, (54.2 + 54.0), (53.0 + 52.9), 52.5, (48.5 + 48.0), 45.7, (28.5 + 28.3). HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_4$: *m*/*z* 356.1731. Found: *m*/*z* 356.1737. Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.95; H, 6.99; N, 7.40. Contains 2.52% toluene.

4-{2-Cyclohexylsulfanylphenyl}piperazine-1-carboxylic Acid Methyl Ester (35a). This compound was cleaved from resin **26a** (2.55 g, 2.16 mmol) to give 555 mg (77%) of crude **35a** as a dark oil (LC-MS: UV 80%, ELSD 92%, R_t = 3.94). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:20)] gave 405 mg (56%) of pale oil (LC-MS: UV 99%, ELSD 99%). ^{1}H NMR: δ 7.26 (dd, 1H, J = 8.0, 1.4), 7.13 (td, 1H, J = 7.5, 1.4), 7.04 (td, 1H, J = 7.5, 1.4), 6.98

(dd, 1H, J = 8.0, 1.4), 3.73 (s, 3H), 3.63 (m, 4H), 3.27 (m, 1H), 2.97 (m, 4H), 2.03 (m, 2H), 1.80 (m, 2H), 1.65 (m, 1H), 1.30 (m, 5H). ^{13}C NMR: δ 156.5, 151.2, 132.5, 129.3, 126.4, 124.6, 120.3, 53.0, 51.9, 44.7, 44.0, 33.7, 26.6, 26.3. HRMALDI-FTMS calcd for $C_{18}H_{26}N_2O_2S + H^+$: m/z 335.1788. Found: m/z 335.1782. Anal. Calcd for $C_{18}H_{26}N_2O_2S$: C, 64.64; H, 7.84; N, 8.38. Found: C, 64.64; H, 7.78; N, 8.24.

4-{3-Cyclohexylsulfanylphenyl}piperazine-1-carboxylic Acid Methyl Ester (35b). This compound was cleaved from resin **26b** (2.52 g, 2.13 mmol) to give 615 mg (86%) of crude **35b** as a dark oil (LC-MS: UV 75%, ELSD 91%, R_t = 3.69). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:20)] gave 411 mg (58%) of pale oil (LC-MS: UV 80%, ELSD 98%). ^{1}H NMR: δ 7.18 (t, 1H, J = 8.0), 6.96 (t, 1H, J = 1.9), 6.92 (m, 1H), 6.77 (m, 1H), 3.73 (s, 3H), 3.62 (m, 4H), 3.14 (m, 4H), 3.09 (m, 1H), 1.98 (m, 2H), 1.77 (m, 2H), 1.61 (m, 1H), 1.31 (m, 5H). ^{13}C NMR: δ 155.4, 151.8, 136.5, 129.8, 123.9, 120.4, 115.4, 53.1, 49.6, 47.0, 44.1, 33.8, 26.4, 26.2. HRMALDI-FTMS calcd for $C_{18}H_{26}N_2O_2S$: m/z 334.1710. Found: m/z 334.1711. Anal. Calcd for $C_{18}H_{26}N_2O_2S$: C, 64.64; H, 7.83; N, 8.38. Found: C, 63.78; H, 7.80; N, 8.21. Contains 1.33% H_2O.

4-{4-Cyclohexylsulfanylphenyl}piperazine-1-carboxylic Acid Methyl Ester (35c). This compound was cleaved from resin **26c** (2.61 g, 2.21 mmol) to give 604 mg (82%) of crude **35c** as a dark solid (LC-MS: UV 83%, ELSD 98%, R_t = 3.69). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:20)] gave 415 mg (56%) of pale solid (LC-MS: UV 95%, ELSD 98%); mp 104−105 °C (Et_2O/heptan). ^{1}H NMR: δ 7.35 (m, 2H), 6.83 (m, 2H), 3.73 (s, 3H), 3.62 (m, 4H), 3.15 (m, 4H), 2.90 (m, 1H), 1.93 (m, 2H), 1.75 (m, 2H), 1.58 (m, 1H), 1.27 (m, 5H). ^{13}C NMR: δ 153.2, 149.7, 134.4, 123.6, 115.8, 52.0, 48.2, 47.1, 42.9, 32.7, 25.4, 25.1. HRMALDI-FTMS calcd for $C_{18}H_{26}N_2O_2S$: m/z 334.1710. Found: m/z 334.1706. Anal. Calcd for $C_{18}H_{26}N_2O_2S$: C, 64.64; H, 7.84; N, 8.38; S, 9.59. Found: C, 64.61; H, 7.89; N, 8.43; S, 9.30.

4-{3-Cyclohexylsulfanyl-2-methylphenyl}piperazine-1-carboxylic Acid Methyl Ester (35d). This compound was cleaved from resin **26d** (2.46 g, 2.06 mmol) to give 548 mg (76%) of crude **35d** as a dark solid (LC-MS: UV 90%, ELSD 98%, R_t = 4.23). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:20)] gave 333 mg (46%) of pale solid (LC-MS: UV 93%, ELSD 96%); mp 109−110 °C (Et_2O/heptane). ^{1}H NMR: δ 7.13 (m, 1H), 7.10 (t, 1H), 6.87 (m, 1H), 3.73 (s, 3H), 3.60 (m, 4H), 3.11 (m, 1H), 2.83 (m, 4H), 2.39 (s, 3H), 1.99 (m, 2H), 1.78 (m, 2H), 1.62 (m, 1H), 1.34 (m, 5H). ^{13}C NMR: δ 156.4, 152.3, 137.1, 134.0, 126.6, 126.3, 117.6, 53.0, 52.4, 46.2, 44.7, 33.8, 26.5, 26.2, 15.8. HRMALDI-FTMS calcd for $C_{19}H_{28}N_2O_2S + H^+$: m/z 349.1944. Found: m/z 349.1941. Anal. Calcd for $C_{19}H_{28}N_2O_2S$: C, 65.48; H, 8.10; N, 8.04; S, 9.20. Found: C, 65.27; H, 8.15; N, 8.05; S, 8.98.

4-{2-(Adamantan-1-ylsulfanyl)phenyl}piperazine-1-carboxylic Acid Methyl Ester (36a). This compound was cleaved from resin **27a** (2.65 g, 2.15 mmol) to give 571 mg (69%) of crude **36a** as a dark solid (LC-MS: UV 86%, ELSD 98%, R_t = 4.51). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:20)] gave 439 mg (53%) of a pale solid (LC-MS: UV 94%, ELSD 100%); mp 140−141 °C (CH_2Cl_2/Et_2O/heptane). ^{1}H NMR: δ 7.49 (dd, 1H, J = 7.5, 1.9), 7.30 (ddd, 1H, J = 7.5, 1.9, 1.4), 6.99 (ddd, 1H, J = 7.1, 3.8, 1.4), 6.96 (dd, 1H, J = 3.8, 1.4), 3.73 (s, 3H), 3.64 (m, 4H), 3.03 (m, 4H), 1.98 (m, 3H), 1.82 (m, 6H), 1.61 (m, 6H). ^{13}C NMR: δ 156.5, 156.1, 140.6, 129.9, 125.6, 122.7, 119.4, 52.5, 52.3, 49.3, 43.9, 43.9, 36.2, 30.0. HRMALDI-FTMS calcd for $C_{22}H_{30}N_2O_2S + H^+$: m/z 387.2101. Found: m/z 387.2110. Anal. Calcd for $C_{22}H_{30}N_2O_2S$: C, 68.36; H, 7.82; N, 7.25; S, 8.29. Found: C, 68.39; H, 7.96; N, 7.27, S, 8.03.

4-[3-(Adamantan-1-ylsulfanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (36b). This compound was cleaved from resin **27b** (2.69 g, 2.18 mmol) to give 723 mg (86%) of crude **36b** as a dark oil (LC-MS: UV 94%, ELSD 97%, R_t = 4.30). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:20)] gave 586 mg (70%) of pale solid (LC-MS: UV 97%, ELSD 100%); mp 89−90 °C (Et_2O/heptane). ^{1}H NMR: δ 7.21 (t, 1H, J = 8.0), 7.04 (m, 2H), 6.92 (m, 1H), 3.73 (s, 3H), 3.64 (m, 4H), 3.16 (m, 4H), 2.01 (m, 3H), 1.82 (m, 6H), 1.62 (m, 6H). ^{13}C NMR: δ 155.8, 150.9, 131.3, 129.3, 128.7, 125.6, 116.7, 52.6, 49.2, 47.8, 43.6, 43.6, 36.1, 29.9. HRMALDI-FTMS calcd for $C_{22}H_{30}N_2O_2S$: m/z 386.2023. Found: m/z 386.2041. Anal. Calcd for $C_{22}H_{30}N_2O_2S$: C, 68.36; H, 7.82; N, 7.25; S, 8.29. Found: C, 68.29; H, 7.90; N, 7.33, S, 8.09.

4-[4-(Adamantan-1-ylsulfanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (36c). This compound was cleaved from resin **27c** (2.67 g, 2.17 mmol) to give 645 mg (77%) of crude **36c** as a dark solid (LC-MS: UV 89%, ELSD 99%, R_t = 4.30). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:10) gave 449 mg (54%) of pale solid (LC-MS: UV 98%, ELSD 99%); mp 126−127 °C (CH_2Cl_2/Et_2O/heptane). ^{1}H NMR: δ 7.37 (m, 2H), 6.84 (m, 2H), 3.73 (s, 3H), 3.63 (m, 4H), 3.20 (m, 4H), 2.00 (m, 3H), 1.78 (m, 6H), 1.61 (m, 6H). ^{13}C NMR: δ 155.8, 151.0, 138.6, 120.3, 115.6, 52.6, 48.5, 47.4, 43.5, 43.4, 36.1, 29.9. HRMALDI-FTMS calcd for $C_{22}H_{30}N_2O_2S + H^+$: m/z 387.2101. Found: m/z 387.2112. Anal. Calcd for $C_{22}H_{30}N_2O_2S$: C, 68.36; H, 7.82; N, 7.25; S, 8.29. Found: C, 68.44; H, 7.89; N, 7.32, S, 8.16.

4-[3-(Adamantan-1-ylsulfanyl)-2-methylphenyl]piperazine-1-carboxylic Acid Methyl Ester (36d). This compound was cleaved from resin **27d** (2.68 g, 2.15 mmol) to give 590 mg (69%) of crude **36d** as a dark solid (LC-MS: UV 89%, ELSD 99%, R_t = 4.64). Purification by chromatography [heptane/EtOAc (90:10) → heptane/EtOAc (30:10)] gave 439 mg (51%) of pale solid (LC-MS: UV 100%, ELSD 99%); mp 165−166 °C (Et_2O/heptane). ^{1}H NMR: δ 7.30 (m, 1H), 7.11 (dd, 1H, J = 8.0, 7.5), 7.02 (m, 1H), 3.74 (s, 3H), 3.60 (m, 4H), 2.85 (m, 4H), 2.52 (s, 3H), 2.00 (m, 3H), 1.85 (m, 6H), 1.62 (m, 6H). ^{13}C NMR: δ 156.4, 152.4, 139.7, 135.1, 132.3, 125.8, 120.4, 53.1, 52.4, 49.9, 44.7, 44.2, 36.6, 30.4, 17.5. HRMALDI-FTMS calcd for $C_{23}H_{32}N_2O_2S + H^+$: m/z 401.2257. Found: m/z 401.2270. Anal. Calcd for $C_{23}H_{32}N_2O_2S$: C, 68.96; H, 8.05; N, 6.99; S, 8.00. Found: C, 68.93; H, 8.19; N, 6.99, S, 7.80.

4-[2-(Adamantan-1-ylsulfanyl)-2-methylphenyl]-[1,4]-diazepane-1-carboxylic Acid Methyl Ester (36e). This compound was cleaved from resin **27e** (2.63 g, 1.84 mmol) to give 474 mg (64%) of crude **36e** as a dark solid (LC-MS: UV 69%, ELSD 99%, R_t = 3.82). Purification by chromatography [toluene/EtOAc (40:1)] gave 256 mg (35%) of pale solid (LC-MS: UV 97%, ELSD 98%); mp 104−105 °C (acetone/heptane). ^{1}H NMR: δ 7.48 (m, 1H), 7.25 (m, 1H), 7.04 (m, 1H), 6.93 (m, 1H), 3.72 (s, 3H), 3.67 (m, 2H), 3.61 (m, 2H), 3.24 (m, 2H), 3.19 (m, 2H), 2.06 (m, 2H), 1.98 (s, 3H), 1.82 (s, 6H), 1.61 (m, 6H). ^{13}C NMR: δ 158.6, (156.8 + 156.7), (140.7 + 140.6), 129.7, (125.4 + 125.3), 122.1, (120.9 + 120.8), (56.7 + 56.4), (56.1 + 55.6), 52.5, 49.4, (48.2 + 47.8), 45.9, 43.9, 36.3, 30.1, 28.9. HRMALDI-FTMS calcd for $C_{23}H_{32}N_2O_2S + H^+$: m/z 401.2257. Found: m/z 401.2244. Anal. Calcd for $C_{23}H_{32}N_2O_2S$: C, 68.96; H, 8.05; N, 6.99. Found: C, 68.73; H, 8.18; N, 7.09.

4-[2-(3-Methoxyphenylsulfanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (37a). This compound was cleaved from resin **28a** (2.52 g, 2.09 mmol) to give 724 mg (97%) of crude **37a** as a dark oil (LC-MS: UV 96%, ELSD 99%, R_t = 3.53). Purification by chromatography [heptane → heptane/EtOAc (80:20)] gave 537 mg (72%) of pale oil (LC-MS: UV 99%, ELSD 100%). ^{1}H NMR: δ 7.26 (t, 1H, J = 8.0), 7.15 (m, 1H), 7.02 (m, 2H), 6.97 (m, 3H), 6.86 (m, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 3.59 (m, 4H), 3.00 (m, 4H). ^{13}C NMR: δ 161.0, 156.8, 150.8, 135.8, 134.2, 130.9, 130.3, 127.7, 126.1, 125.5, 121.0, 118.9, 114.6, 56.1, 53.4, 52.4, 45.0. HRMALDI-FTMS calcd for $C_{19}H_{22}N_2O_3S + H^+$: m/z 359.1424. Found: m/z 359.1407. Anal. Calcd for $C_{19}H_{22}N_2O_3S$: C, 63.66; H, 6.19; N, 7.81; S, 8.94. Found: C, 63.61; H, 6.34; N, 7.74, S, 9.10.

4-[3-(3-Methoxyphenylsulfanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (37b). This compound was cleaved from resin **28b** (2.56 g, 2.12 mmol) to give 743 mg

(98%) of crude **37b** as a dark oil (LC-MS: UV 95%, ELSD 99%, R_t = 3.32). Purification by chromatography [heptane → heptane/EtOAc (80:20)] gave 540 mg (71%) of pale solid (LC-MS: UV 98%, ELSD 100%); mp 95−96 °C (Et_2O/heptane). ^{1}H NMR: δ 7.20 (t, 2H, J = 8.0), 6.94 (m, 1H), 6.90 (m, 1H), 6.85 (m, 2H), 6.79 (m, 1H), 6.76 (m, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.60 (m, 4H), 3.11 (m, 4H). ^{13}C NMR: δ 160.0, 155.8, 151.7, 137.2, 136.0, 129.9, 129.8, 123.1, 122.8, 119.2, 115.8, 115.5, 112.6, 55.2, 52.6, 49.0, 43.6. HRMALDI-FTMS calcd for $C_{19}H_{22}N_2O_3S + H^+$: m/z 359.1424. Found: m/z 359.1421. Anal. Calcd for $C_{19}H_{22}N_2O_3S$: C, 63.66; H, 6.19; N, 7.81; S, 8.94. Found: C, 63.59; H, 6.29; N, 7.79, S, 8.89.

4-[4-(3-Methoxyphenylsulfanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (37c). This compound was cleaved from resin **28c** (2.71 g, 2.25 mmol) to give 743 mg (92%) of crude **37c** as a dark oil (LC-MS: UV 93%, ELSD 99%, R_t = 3.32). Purification by chromatography [heptane → heptane/EtOAc (75:25)] gave 522 mg (65%) of pale solid (LC-MS: UV 98%, ELSD 100%); mp 88−89 °C (Et_2O/heptane). ^{1}H NMR: δ 7.39 (m, 2H), 7.13 (t, 1H, J = 8.0), 6.89 (m, 2H), 6.74 (m, 1H), 6.71 (m, 1H), 6.67 (m, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.63 (m, 4H), 3.12 (m, 4H). ^{13}C NMR: δ 160.0, 155.9, 151.1, 140.3, 135.3, 129.7, 122.7, 120.3, 116.9, 113.5, 111.3, 55.2, 52.7, 48.7, 43.6. HRMALDI-FTMS calcd for $C_{19}H_{22}N_2O_3S$: m/z 358.1346. Found: m/z 358.1353. Anal. Calcd for $C_{19}H_{22}N_2O_3S$: C, 63.66; H, 6.19; N, 7.81; S, 8.94. Found: C, 63.63; H, 6.30; N, 7.90, S, 8.88.

4-[3-(3-Methoxyphenylsulfanyl)-2-methylphenyl]piperazine-1-carboxylic Acid Methyl Ester (37d). This compound was cleaved from resin **28d** (2.63 g, 2.16 mmol) to give 744 mg (93%) of crude **37d** as a dark oil (LC-MS: UV 95%, ELSD 99%, R_t = 3.78). Purification by chromatography [heptane → heptane/EtOAc (80:20)] gave 509 mg (63%) of pale oil (LC-MS: UV 99%, ELSD 99%). ^{1}H NMR: δ 7.18 (dd, 1H, J = 8.0, 7.5), 7.10 (dd, 1H, J = 8.0, 7.5), 7.05 (dd, 1H, J = 7.5, 1.4), 6.95 (dd, 1H, J = 8.0, 1.4), 6.80 (m, 1H), 6.77 (m, 1H), 6.75 (m, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.62 (m, 4H), 2.85 (m, 4H), 2.38 (s, 3H). ^{13}C NMR: δ 160.5, 156.4, 152.6, 137.7, 136.0, 134.9, 130.3, 128.3, 127.2, 122.7, 119.2, 115.7, 112.7, 55.6, 53.0, 52.3, 44.7, 15.8. HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_3S + H^+$: m/z 373.1581. Found: m/z 373.1576. Anal. Calcd for $C_{20}H_{24}N_2O_3S$: C, 64.49; H, 6.49; N, 7.52; S, 8.61. Found: C, 64.59; H, 6.71; N, 7.45, S, 8.43.

4-[2-(3-Methoxyphenylsulfanyl)-2-methylphenyl]-[1,4]-diazepane-1-carboxylic Acid Methyl Ester (37e). This compound was cleaved from resin **28e** (2.74 g, 1.95 mmol) to give 538 mg (74%) of crude **37e** as a dark oil (LC-MS: UV 92%, ELSD 99%, R_t = 3.60). Purification by chromatography [toluene/EtOAc (30:1)] gave 365 mg (50%) of pale oil (LC-MS: UV 93%, ELSD 98%). ^{1}H NMR: δ 7.25 (m, 1H), 7.13 (m, 1H), 7.07 (m, 1H), 6.98 (m, 1H), 6.93 (m, 3H), 6.84 (m, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 3.68 (m, 1H), 3.61 (m, 2H), 3.55 (m, 1H), 3.16 (m, 4H), 1.98 (m, 2H). ^{13}C NMR: δ 160.2, (156.9 + 156.7), (152.7 + 152.5), (135.6 + 135.5), (133.6 + 133.4), 130.0, (129.8 + 129.7), (127.0 + 126.9), (125.0 + 124.9), 124.3, 121.9, (117.8 + 117.7), 113.6, 56.6, 55.3, 52.5, 48.5, 48.1, (46.0 + 45.8), (28.9 + 28.7). HRMALDI-FTMS calcd for $C_{20}H_{24}N_2O_3S + H^+$: m/z 373.1581. Found: m/z 373.1563. Anal. Calcd for $C_{20}H_{24}N_2O_3S$: C, 64.49; H, 6.49; N, 7.52. Found: C, 64.66; H, 6.58; N, 7.54.

4-[2-(4-*tert*-Butylphenylselanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (38a). This compound was cleaved from resin **29a** (2.62 g, 2.05 mmol) to give 762 mg (86%) of crude **38a** as a dark oil (LC-MS: UV 75%, ELSD 99%, R_t = 4.55). Purification by chromatography [toluene/EtOAc (30:1)] gave 621 mg (70%) of pale solid (LC-MS: UV 99%, ELSD 100%); mp 107−108 °C (acetone/heptane). ^{1}H NMR: δ 7.55 (m, 2H), 7.39 (m, 2H), 7.12 (ddd, 1H, J = 7.5, J 7.1, 1.4), 7.04 (dd, 1H, J = 7.5, 1.4), 6.91 (ddd, 1H, J = 8.0, 7.1, 1.0), 6.82 (dd, 1H, J = 7.5, 1.4), 3.74 (s, 3H), 3.65 (m, 4H), 2.97 (m, 4H), 1.34 (s, 9H). ^{13}C NMR: δ 156.1, 151.9, 149.7, 136.5, 133.5, 128.7, 126.7, 126.4, 125.7, 124.5, 120.7, 52.6, 52.1, 44.4, 34.7, 31.3. HRMALDI-FTMS calcd for $C_{22}H_{28}N_2O_2Se + H^+$: m/z 433.1389. Found: m/z 433.1396. Anal. Calcd for $C_{22}H_{28}N_2O_2Se$: C, 61.25; H, 6.54; N, 6.49. Found: C, 61.33; H, 6.44; N, 6.48.

4-[3-(4-*tert*-Butylphenylselanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (38b). This compound was cleaved from resin **29b** (2.72 g, 2.13 mmol) to give 735 mg (80%) of crude **38b** as a dark oil (LC-MS: UV 89%, ELSD 85%, R_t = 4.22). Purification by chromatography [toluene/EtOAc (30:1)] gave 555 mg (61%) of pale oil (LC-MS: UV 96%, ELSD 100%). ^{1}H NMR: δ 7.41 (m, 2H), 7.34 (m, 2H), 7.15 (t, 1H, J = 8.01), 7.01 (t, 1H, J = 1.4), 6.94 (m, 1H), 6.79 (m, 1H), 3.72 (s, 3H), 3.59 (m, 4H), 3.10 (m, 4H), 1.30 (s, 9H). ^{13}C NMR: δ 155.9, 151.7, 150.7, 133.1, 132.4, 129.8, 127.3, 126.4, 124.4, 120.5, 115.3, 52.7, 49.0, 43.6, 34.6, 31.3. HRMALDI-FTMS calcd for $C_{22}H_{28}N_2O_2Se + H^+$: m/z 433.1389. Found: m/z 433.1383. Anal. Calcd $C_{22}H_{28}N_2O_2Se$: C, 61.25; H, 6.54; N, 6.49. Found: C, 60.33; H, 6.45; N, 6.19. Contains 1.44% H_2O.

4-[4-(4-*tert*-Butylphenylselanyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (38c). This compound was cleaved from resin **29c** (2.64 g, 2.07 mmol) to give 774 mg (87%) of crude **38c** as a dark oil (LC-MS: UV 74%, ELSD 97%, R_t = 4.26). Purification by chromatography [toluene/EtOAc (30:1)] gave 484 mg (54%) of pale solid (LC-MS: UV 94%, ELSD 100%); mp 96−98 °C (acetone/heptane). ^{1}H NMR: δ 7.46 (m, 2H), 7.27 (m, 2H), 7.24 (m, 2H), 6.83 (m, 2H), 3.73 (s, 3H), 3.62 (m, 4H), 3.16 (m, 4H), 1.28 (s, 9H). ^{13}C NMR: δ 154.4, 149.3, 148.3, 134.3, 129.6, 127.8, 124.7, 118.2, 115.6, 51.2, 47.3, 42.1, 33.0, 29.8. HRMALDI-FTMS calcd for $C_{22}H_{28}N_2O_2Se + H^+$: m/z 433.1389. Found: m/z 433.1385. Anal. Calcd for $C_{22}H_{28}N_2O_2Se$: C, 61.25; H, 6.54; N, 6.49. Found: C, 61.26; H, 6.57; N, 6.55.

4-{2-Methyl-3-(4-*tert*-butylphenylselanyl)phenyl}-piperazine-1-carboxylic Acid Methyl Ester (38d). This compound was cleaved from resin **29d** (2.78 g, 2.15 mmol) to give 630 mg (66%) of crude **38d** as a dark solid (LC-MS: UV 80%, ELSD 100%, R_t = 4.76). Purification by chromatography [toluene/EtOAc (30:1)] gave 431 mg (45%) of pale solid (LC-MS: UV 92%, ELSD 100%); mp 127−129 °C (acetone/heptane). ^{1}H NMR: δ 7.41 (ddd, 2H, J = 8.5, 2.4, 1.9), 7.32 (ddd, 2H, J = 8.5, 2.4, 1.9), 7.00 (dd, 1H, J = 8.0, 7.5), 6.95 (dd, 1H, J = 8.0, 1.4), 6.89 (dd, 1H, J = 8.0, 1.4), 3.73 (s, 3H), 3.62 (m, 4H), 2.84 (m, 4H), 2.40 (s, 3H), 1.31 (s, 9H). ^{13}C NMR: δ 156.0, 151.8, 151.0, 135.0, 134.0, 133.3, 127.3, 126.8, 126.6, 126.3, 117.9, 52.6, 52.0, 44.3, 34.6, 31.3, 17.0. HRMALDI-FTMS calcd for $C_{23}H_{30}N_2O_2Se + H^+$: m/z 447.1545. Found: m/z 447.1546. Anal. Calcd for $C_{23}H_{30}N_2O_2Se$: C, 62.01; H, 6.79; N, 6.29. Found: C, 61.77; H, 6.91; N, 6.55.

4-[2-(4-*tert*-Butylphenylselanyl)phenyl]-[1,4]diazepane-1-carboxylic Acid Methyl Ester (38e). This compound was cleaved from resin **29e** (2.79 g, 1.89 mmol) to give 609 mg (80%) of crude **38e** as a dark oil (LC-MS: UV 81%, ELSD 100%, R_t = 4.55). Purification by chromatography [toluene/EtOAc (30:1)] gave 475 mg (57%) of pale solid (LC-MS: UV 96%, ELSD 99%); mp 115−117 °C (acetone/heptane). ^{1}H NMR: δ 7.56 (ddd, 2H, J = 8.5, 2.4, 1.9), 7.38 (ddd, 2H, J = 8.5, 2.4, 1.9), 7.07 (m, 2H), 6.88 (ddd, 1H, J = 8.0, 1.9, 1.4), 6.78 (dd, 1H, J = 8.0, 1.4), 3.73 (s, 3H), 3.67 (m, 4H), 3.13 (m, 4H), 2.03 (m, 2H), 1.35 (s, 9H). ^{13}C NMR: δ (156.9 + 156.7), (152.2 + 152.1), 151.8, 136.5, (134.2 + 134.1), 128.2, 126.7, 126.2, 125.5, 124.8, 122.3, (57.3 + 57.2), (55.9 + 55.8), 52.6, (48.5 + 48.1), (46.1 + 45.9), 34.7, 31.3, (29.1 + 28.9). HRMALDI-FTMS calcd for $C_{23}H_{30}N_2O_2Se + H^+$: m/z 447.1545. Found: m/z 447.1549. Anal. Calcd for $C_{23}H_{30}N_2O_2Se$: C, 62.01; H, 6.79; N, 6.29. Found: C, 61.71; H, 7.02; N, 6.37.

4-{2-[4-(10,10-Dimethyl-9,10-dihydroanthracen-9-yl)piperidin-1-yl]phenyl}piperazine-1-carboxylic Acid Methyl Ester (39a). This compound was cleaved from resin **30a** (2.53 g, 1.86 mmol) to give 537 mg (57%) of crude **39a** as a dark oil (LC-MS: UV 69%, ELSD 90%, R_t = 2.95). Purification by chromatography [heptane → heptane/EtOAc (95:5)] gave

103 mg (11%) of pale oil (LC-MS: UV 94%, ELSD 99%). ^{1}H NMR: δ 7.57 (d, 2H, J = 7.5), 7.29 (m, 2H), 7.21 (m, 4H), 6.90 (m, 2H), 6.80 (m, 2H), 3.78 (d, 1H, J = 7.1), 3.76 (s, 3H), 3.56 (m, 6H), 3.04 (m, 4H), 2.27 (m, 2H), 1.73 (s, 3H), 1.68 (s, 3H), 1.61 (m, 2H), 1.55 (m, 1H), 1.37 (m, 2H). ^{13}C NMR: δ 156.5, 146.1, 145.1, 144.9, 137.1, 129.7, 127.0, 126.6, 125.6, 123.6, 123.1, 119.4, 118.8, 53.0, 51.2, 49.9, 46.4, 44.9, 41.4, 39.2, 35.6, 32.8, 32.1. HRMALDI-FTMS calcd for $C_{33}H_{39}N_3O_2 + H^+$: m/z 510.3115. Found: m/z 510.3110. Anal. Calcd for $C_{33}H_{39}N_3O_2$: C, 77.77; H, 7.71; N, 8.24. Found: C: 76.03; H, 7.76; N, 8.09. Contains 2.25% H_2O.

4-{3-[4-(10,10-Dimethyl-9,10-dihydroanthracen-9-yl)piperidin-1-yl]phenyl}piperazine-1-carboxylic Acid Methyl Ester (39b). This compound was cleaved from resin **30b** (2.91 g, 2.15 mmol) to give 921 mg (84%) of crude **39b** as a dark oil (LC-MS: UV 72%, ELSD 99%, R_t = 2.70). Purification by chromatography [heptane → heptane/EtOAc (95:5)] gave 590 mg (54%) of pale oil (LC-MS: UV 84%, ELSD 99%). ^{1}H NMR: δ 7.56 (d, 2H, J = 8.0), 7.28 (m, 2H), 7.19 (m, 4H), 7.09 (t, 1H, J = 8.5), 6.40 (m, 3H), 3.80 (d, 1H, J = 6.6), 3.71 (s, 3H), 3.58 (m, 6H), 3.07 (m, 4H), 2.43 (m, 2H), 1.72 (s, 3H), 1.67 (s, 3H), 1.61 (m, 2H), 1.55 (m, 1H), 1.43 (m, 2H). ^{13}C NMR: δ 156.3, 153.3, 152.6, 144.8, 136.9, 129.9, 129.7, 127.0, 126.6, 125.6, 109.7, 108.9, 106.3, 53.0, 51.1, 50.9, 50.1, 46.5, 44.2, 39.1, 35.5, 32.8, 31.2. HRMALDI-FTMS calcd for $C_{33}H_{39}N_3O_2 + H^+$: m/z 510.3115. Found: m/z 510.3123. Anal. Calcd for $C_{33}H_{39}N_3O_2$: C, 77.77; H, 7.71; N, 8.24. Found: C, 77.61; H, 8.00; N, 8.10.

4-{4-[4-(10,10-Dimethyl-9,10-dihydroanthracen-9-yl)piperidin-1-yl]phenyl}piperazine-1-carboxylic Acid Methyl Ester (39c). This compound was cleaved from resin **30c** (2.92 g, 2.15 mmol) to give 892 mg (81%) of crude **39c** as a dark oil (LC-MS: UV 78%, ELSD 99%, R_t = 2.56). Purification by chromatography [heptane → heptane/EtOAc (95:5)] gave 582 mg (53%) of pale solid (LC-MS: UV 94%, ELSD 99%); mp 155−154 °C (Et_2O/heptane). ^{1}H NMR: δ 7.57 (d, 2H, J = 7.54), 7.28 (m, 2H), 7.20 (m, 4H), 6.81 (m, 4H), 3.80 (d, 1H, J = 6.1), 3.71 (s, 3H), 3.59 (m, 4H), 3.47 (m, 2H), 3.00 (m, 4H), 2.37 (m, 2H), 1.72 (s, 3H), 1.67 (s, 3H), 1.61 (m, 2H), 1.52 (m, 1H), 1.45 (m, 2H). ^{13}C NMR: δ 156.0, 146.5, 145.0, 144.5, 136.6, 129.3, 126.6, 126.2, 125.2, 118.3, 118.1, 52.6, 51.5, 50.6, 50.5, 45.9, 43.9, 38.7, 35.2, 32.4, 30.9. HRMALDI-FTMS calcd for $C_{33}H_{39}N_3O_2$: m/z 509.3037. Found: m/z 509.3035. Anal. Calcd for $C_{33}H_{39}N_3O_2$: C, 77.77; H, 7.71; N, 8.24. Found: C, 77.46; H, 7.73; N, 8.77.

4-{3-[4-(10,10-Dimethyl-9,10-dihydroanthracen-9-yl)piperidin-1-yl]-2-methylphenyl}piperazine-1-carboxylic Acid Methyl Ester (39d). This compound was cleaved from resin **30d** (2.84 g, 2.07 mmol) to give 856 mg (79%) of crude **39d** as a dark oil (LC-MS: UV 82%, ELSD 98%, R_t = 3.45). Purification by chromatography [heptane → heptane/EtOAc (95:5)] gave 530 mg (49%) of pale solid (LC-MS: UV 98%, ELSD 100%); mp 197−198 °C (Et_2O/heptane). ^{1}H NMR: δ 7.58 (d, 2H, J = 7.5), 7.28 (m, 2H), 7.21 (m, 4H), 7.05 (t, 1H, J = 8.0), 6.66 (m, 2H), 3.79 (d, 1H, J = 6.1), 3.72 (s, 3H), 3.59 (m, 4H), 3.05 (m, 2H), 2.83 (m, 4H), 2.37 (m, 2H), 2.24 (s, 3H), 1.74 (s, 3H), 1.67 (s, 3H), 1.59 (m, 2H), 1.50 (m, 3H). ^{13}C NMR: δ 156.4, 154.0, 152.7, 144.9, 137.3, 129.8, 127.5, 126.9, 126.7, 126.5, 125.6, 114.7, 113.9, 53.4, 53.0, 52.2, 51.4, 46.4, 44.8, 39.2, 35.8, 32.4, 32.1, 13.6. HRMALDI-FTMS calcd for $C_{34}H_{41}N_3O_2 + H^+$: m/z 524.3272. Found: m/z 524.3186. Anal. Calcd for $C_{34}H_{41}N_3O_2$: C, 77.98; H, 7.89; N, 8.02. Found: C, 77.91; H, 7.97; N, 8.49.

4-{2-[4-(10,10-Dimethyl-9,10-dihydroanthracen-9-yl)piperidin-1-yl]phenyl}-[1,4]diazepane-1-carboxylic Acid Methyl Ester (39e). This compound was cleaved from resin **30e** (2.38 g, 1.53 mmol) to give 335 mg (42%) of crude **39e** as a dark oil (LC-MS: UV 1%, ELSD 9%, R_t = 2.80). Purification by chromatography [toluene/EtOAc (40:1)] gave 8 mg (1%) of pale oil (LC-MS: UV 76%, ELSD 99%). ^{1}H NMR: δ 7.57 (m, 2H), 7.29 (m, 2H), 7.23 (m, 2H), 7.19 (m, 2H), 6.87 (m, 3H), 6.81 (m, 1H), 3.80 (m, 1H), 3.74 (m, 3H), 3.61 (m, 2H), 3.53 (m, 2H), 3.42 (m, 2H), 3.27 (m, 2H), 3.19 (m, 2H), 2.28 (m, 2H), 1.89 (m, 2H), 1.73 (s, 3H), 1.68 (s, 3H), 1.58 (m, 3H), 1.43 (m, 2H). ^{13}C NMR: δ (156.9 + 156.7), 146.8, 146.1, 144.5, (136.8 + 136.7), 129.3, 126.5, 126.2, 125.3, 122.8, (122.7 + 122.6), 120.2, 119.4, (54.2 + 54.0), (53.4 + 53.3), (52.6 + 52.5), 51.3, 50.7, 48.3, 47.8, 46.1, 46.0, 38.8, 35.2, (32.5 + 32.4), 31.5. HRMALDI-FTMS calcd for $C_{34}H_{41}N_3O_2 + H^+$: m/z 524.3272. Found: m/z 524.3253.

4-[2-(Diphenylphosphinoyl)phenyl]piperazine-1-carboxylic Acid Methyl Ester (40a). This compound was cleaved from resin **31a** (2.59 g, 2.05 mmol) to give 685 mg (80%) of crude **40a** as a dark solid (LC-MS: UV 72%, ELSD 31%, R_t = 2.68). Purification by chromatography [toluene/acetone (30:10)] gave 173 mg (20%) of pale solid (LC-MS: UV 90%, ELSD 99%); mp 70−105 °C (acetone/heptane). ^{1}H NMR (CD_2Cl_2): δ 7.70 (m, 4H), 7.59 (m, 1H), 7.55 (m, 2H), 7.49 (m, 4H), 7.32 (m, 1H), 7.15 (m, 1H), 7.07 (m, 1H), 3.66 (s, 3H), 3.07 (m, 4H), 2.84 (m, 4H). ^{13}C NMR: δ (158.3 + 158.2), 156.5, 135.9, (135.5 + 135.4), 135.0, 134.3, (132.0 + 131.9), (131.8 + 131.8), (129.1 + 129.0), (125.7 + 125.6). ^{31}P NMR (CD_2Cl_2): δ 26.3. HRMALDI-FTMS calcd for $C_{24}H_{25}N_2O_3P + H^+$: m/z 421.1676. Found: m/z 421.1663.

4-{2-[(Diphenylphosphinyl)selenyl]phenyl}piperazine-1-carboxylic Acid Methyl Ester (41d). This compound was cleaved from resin **32d** (2.59 g, 1.93 mmol) to give 675 mg (70%) of crude **41d** as a dark solid (LC-MS: UV 43%, ELSD 73%, R_t = 3.76). Purification by chromatography [toluene/EtOAc (30:1)] gave 323 mg (11%) of pale solid (LC-MS: UV 98%, ELSD 100%); mp 194−195 °C (acetone/heptane). ^{1}H NMR: δ 7.85 (m, 4H), 7.48 (m, 6H), 7.15 (m, 1H), 7.09 (m, 1H), 6.66 (m, 1H), 3.72 (s, 3H), 3.57 (m, 4H), 2.83 (m, 4H), 2.41 (s, 3H). ^{13}C NMR: δ 156.0, (153.2 + 153.1), (137.7 + 137.6), (132.9 + 132.8), 132.3, 131.6, (128.6 + 128.5), (128.3 + 128.2), (126.2 + 126.1), 123.1, 52.7, 51.9, 44.2, 17.1. ^{31}P NMR (CD_2Cl_2): δ 34.1. ^{77}Se NMR (CD_2Cl_2): δ 81.6. HRMALDI-FTMS calcd for $C_{25}H_{27}N_2O_2PSe + H^+$: m/z 499.1048. Found: m/z 499.1063. Anal. Calcd for $C_{25}H_{27}N_2O_2PSe$: C, 60.36; H, 5.47; N, 5.63. Found: C, 60.17; H, 4.97; N, 5.58.

Acknowledgment. The very skillful technical assistance by Mr. Peter Brøsen and Mr. Erik Damgård is gratefully acknowledged. The proof reading by Dr. Robert Dancer and the preparation of the manuscript by Ms. V. Larsen are highly appreciated. The fruitful discussions with Prof. Mikael Begtrup are gratefully acknowledged.

Supporting Information Available: ^{1}H NMR spectra of representative products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO025721Q