Novel synthetic strategy of carbolines *via* palladium-catalyzed amination and arylation reaction

Takehiko Iwaki, Akito Yasuhara and Takao Sakamoto *

Faculty of Pharmaceutical Sciences, Tohoku University Aoba-ku, Sendai 980-8578, Japan

Received (in Cambridge) 9th February 1999, Accepted 7th April 1999

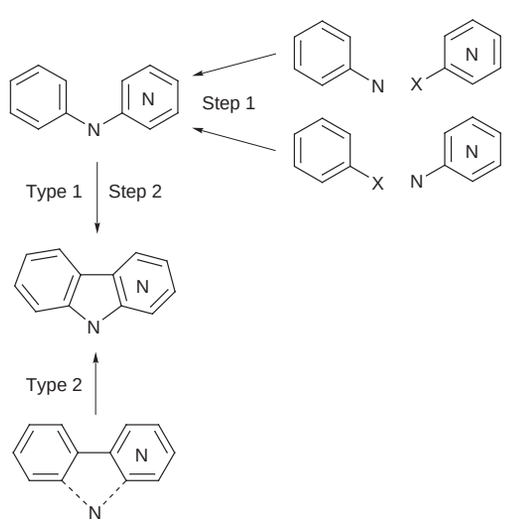
Four parent carbolines and the corresponding 5- or 9-methylsulfonyl derivatives were synthesized by the palladium-catalyzed intramolecular arylation reaction of *ortho*-bromo-substituted anilinopyridines which were prepared by the palladium-catalyzed amination reaction of iodobenzenes with aminopyridines. Carbazole and its 9-methylsulfonyl derivative were also synthesized by the same method.

Introduction

Carbolines (pyrido[x,y-*b*]indoles) are known as the skeletons of naturally occurring compounds, and, particularly, β-carboline (9*H*-pyrido[3,4-*b*]indole) is known as the skeleton of numerous alkaloids. Although many synthetic methods for producing carboline ring systems have been studied,[1] most of them are applications of the Fischer indole cyclization reaction to cyclohexanone pyridinylhydrazones or piperidinone phenylhydrazones and isoquinoline cyclization reactions (*e.g.*, Bischler–Napieralsky or Pictet–Spengler reaction) to indole derivatives. These methods are suitable for partially hydrogenated carbolines, but not very effective for fully aromatic derivatives. In addition, the Fischer cyclization reaction sometimes affords isomers and the synthesis of α- and δ-carbolines is not possible using isoquinoline cyclization reactions. Simple, general, and efficient synthetic methods for the four parent carbolines are scarcely known (to our knowledge) except for Quéguiner's method to be discussed later.

One of the simple and general synthetic methods for fully aromatic carbolines is considered to be the pyrrole-ring construction from benzene and pyridine building blocks. One of the two routes known up to now is the Type 1 route shown in Scheme 1, which is the cyclization reaction of anilinopyridine equivalent derivatives or the ring-transformation reaction of benzo- or pyridotriazoles, and the other one (Type 2 route) is the cyclization reaction of phenylpyridine derivatives which have a nitrogen substituent at an *ortho*-position.

Examples of the Type 1 synthesis are the thermolysis reaction of 1-pyridinylbenzotriazoles[2a–c] or phenylpyridotriazoles,[2d] and the radical cyclization reaction of the aryl radicals generated from the *o*-diazonium derivatives,[2e,f] but these methods have no generality for the synthesis of all carboline skeletons and sometimes gave a mixture of isomers. The Type 2 synthetic methods involve the thermolysis reaction of *o*-pyridinylphenyl azides[3a] or *o*-phenylpyridinyl azides[3b] and the insertion reaction of the arylnitrenes generated from the corresponding nitroso[3c] or nitro derivatives.[3d,e] These methods also have no generality for the synthesis of the four carbolines and sometimes gave the products in low yields. Recently, a general Type 2 method giving high yields was developed by Quéguiner *et al.*[4a–d] who applied their method to the synthesis of natural products. Their method consists of the combination of the palladium-catalyzed cross-coupling reaction of iodofluoropyridines with aminophenylboronic acid derivatives and the intramolecular nucleophilic substitution reaction of the amino group on the benzene ring to the fluoro group of the pyridine ring.



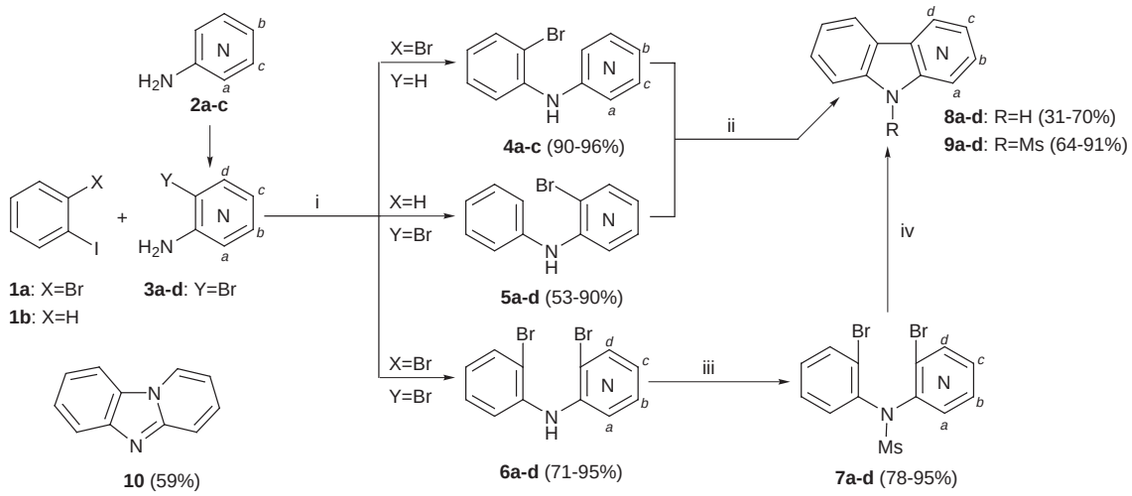
Scheme 1

On the basis of the background described above, we designed a new strategy for the Type 1 synthesis of the four parent carbolines. This strategy consists of the combination of two palladium-catalyzed reactions, namely the amination reaction of iodobenzenes with aminopyridines and the intramolecular arylation reaction of *ortho*-bromo-substituted anilinopyridines.

There are two possible strategies to synthesize *ortho*-bromo-substituted anilinopyridines using the method reported by Buchwald *et al.*[5] (Step 1). These are the palladium-catalyzed reactions of halogenopyridines with aniline derivatives, and of halogenobenzenes with aminopyridines. We chose the latter route, because of the easy availability of the starting compounds and the selectivity of the palladium-catalyzed reaction. As the cyclization reaction to carbolines (Step 2), the palladium-catalyzed intramolecular arylation reactions[6,7] of *ortho*-monohalogenoanilinopyridines and of *ortho*,*ortho'*-dihalogenoanilinopyridines were selected.

Results and discussion

The palladium-catalyzed cross-coupling reaction of 2-bromoiodobenzene **1a** with 2-aminopyridine **2a** under the reported conditions[5a] gave 2-(2-bromoanilino)pyridine **4a** in 95% yield. Analogously, 4- **4b** and 3-(2-bromoanilino)pyridine **4c** were also obtained from the reaction of **1a** with **2b**,**c** in 96 and 90% yield, respectively. Although the cyclization by the intramolecular palladium-catalyzed arylation reaction of **4b**,**c** in the presence of palladium diacetate and sodium carbonate in DMF under reflux conditions gave the corresponding γ-(5*H*-pyrido[4,3-*b*]indole) **8c** and δ-carboline (5*H*-pyrido-



Scheme 2 *Reagents and conditions*: i, $Pd_2(dba)_3$, DPPF, *t*-BuONa, toluene, 100 °C; ii, $Pd(OAc)_2$, Na_2CO_3, DMF, reflux; iii, NaH, MsCl, THF, rt; iv, $PdCl_2(PPh_3)_2$, $(SnBu_3)_2$, Li_2CO_3, Et_4NI, toluene (DMF), reflux. **a** N replaces CH at *a*; **b** N replaces CH at *b*; **c** N replaces CH at *c*; **d** N replaces CH at *d*.

[3,2-*b*]indole) **8d** in 70 and 51% yield, respectively, the cyclization reaction of **4a** gave no α-carboline (9*H*-pyrido[2,3-*b*]-indole) **8a** but, gave instead, the pyrido[1,2-*a*]benzimidazole **10** in 59% yield, which resulted from the cyclization reaction at the pyridine ring nitrogen of **4a** (Scheme 2). Although the yields of **4a**–**c** were satisfactory, this route has some weak points, such as the fact that the starting (2-bromoanilino)pyridines necessary to synthesize all four carbolines were not available, the palladium-catalyzed cyclization reaction of **4a** gave no α-carboline, and the yield of δ-carboline was unsatisfactory.

In order to overcome these weak points, we next examined an alternative route which consists of the cross-coupling reaction of iodobenzene **1b** with *o*-aminobromopyridines **3a**–**d**. This route is suitable for the synthesis of the starting materials for all carbolines and cannot yield the unexpected pyrido-[1,2-*a*]benzimidazole **10**. Moreover, the palladium-catalyzed cyclization reaction of the relatively π-deficient bromopyridine moieties with the relatively π-excessive aniline moiety is expected to proceed smoothly, because the palladium-catalyzed cross-coupling reactions of π-deficient heteroaryl halides with π-excessive heterocycles have been reported.[8]

o-Aminobromopyridines **3a**–**c**, but not 3-amino-2-bromopyridine **3d**, were synthesized by the alkaline hydrolysis reaction of *o*-bromo-(2,2-dimethylpropanoylamino)pyridines which were prepared by the *ortho*-directed lithiation reaction of (2,2-dimethylpropanoylamino)pyridines[9] and subsequent bromination with 1,2-dibromoethane. The palladium-catalyzed cross-coupling reaction of iodobenzene **1b** with 2-amino-3-bromopyridine **3a** under the above mentioned reaction conditions gave 2-anilino-3-bromopyridine **5a** in 90% yield. The analogous cross-coupling reaction of **1b** with 3-amino-2-bromo- **3b**, 4-amino-3-bromo- **3c**, and 3-amino-2-bromopyridine **3d** gave the corresponding anilinobromopyridines **5b**–**d** in 53–88% yield, respectively. The four *o*-anilinobromopyridines **5a**–**d** were subjected to the same conditions as the cyclization reaction of isomers **4a**–**c** to give the corresponding carbolines **8a**–**d** in yields of 31–61%.

As a result, this general route can synthesize all parent carbolines, but the yields of the cyclization reactions were unsatisfactory. In order to improve the yields of the cyclization step, we examined the aforementioned third method. The palladium-catalyzed cross-coupling reaction of 2-bromoiodobenzene **1a** with *o*-aminobromopyridines **3a**–**d** gave *o*,*o*′-dibromoanilinopyridines **6a**–**d** in 71–93% yield. The cyclization reaction to carbolines **9a**–**d** *via* the intermediary tributylstannyl derivatives by reaction with hexabutyldistannane in the presence of dichlorobis(triphenylphosphine)palladium, lithium carbonate, and tetraethylammonium iodide in toluene under reflux conditions[6] did not proceed. Then **6a**–**d** were converted to the corresponding *N*-methylsulfonyl derivatives **7a**–**d** under conventional conditions in yields of 78–95%, and **7a**–**d** were cyclized under the conditions mentioned above to give *N*-methylsulfonyl-α- **9a** and -δ-carboline **9d** in 91 and 84% yield, respectively. However, the β- **9b** and γ-carboline **9c** were hardly formed under these conditions, because of the low solubilities of **7b**,**c** in toluene. Improvements in the yields were achieved using toluene–DMF (10:1) as the solvent, and **9b**,**c** were obtained in 64 and 74% yield, respectively.

Finally, we applied the successful carboline synthesis method to carbazole synthesis. Namely, the palladium-catalyzed reaction of **1a**,**b** with 2-bromoaniline **11b** gave 2-bromo- **12a** and 2,2′-dibromodiphenylamine **12b** in 46 and 96% yield, respectively (Scheme 3). Although the yields (41–47%) of the cyclization reaction were unsatisfactory, carbazole **14a** and 9-(methylsulfonyl)carbazole **14b** were obtained.

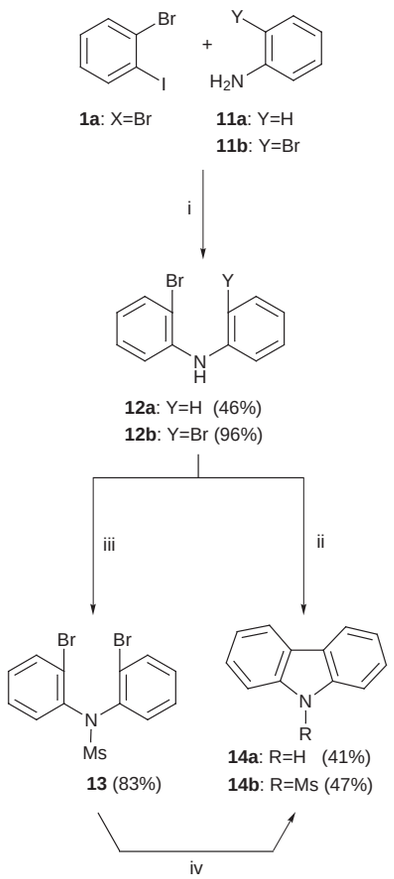
Conclusions

A simple and general method for the synthesis of four parent carbolines and carbazoles was achieved by the combination of two palladium-catalyzed reactions, which are the amination reaction of iodobenzenes with aminopyridines or anilines and the intramolecular biaryl coupling reaction of *ortho*-bromo- and *ortho*,*ortho*′-dibromo-substituted anilinoarenes.

Experimental

General comments

THF and Et_2O were distilled from sodium/benzophenone ketyl before use. n-BuLi was titrated using 2,5-dimethoxybenzyl alcohol before use. All mps (recorded on a YAZAWA micro melting point BY-2 apparatus) and bps are uncorrected. IR spectra were taken on a JASCO IR-810 spectrophotometer. ^{1}H NMR spectra were recorded on Varian Gemini 2000 (300 MHz) and Hitachi R-300 (300 MHz) spectrometers. Chemical shifts are expressed in δ (ppm) values with tetramethylsilane (TMS) as internal reference, and coupling constants (*J*) are expressed in Hz. The following abbreviations are used: s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet, dt = double triplet, br = broad, and br s = broad singlet. Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on JMS-DX303 and JMS-AX500 instruments. 3-Amino-2-bromopyridine **3d** was prepared according to the literature method.[10]



Scheme 3 *Reagents and conditions*: i, $Pd_2(dba)_3$, DPPF, *t*-BuONa, toluene, 100 °C; ii, $Pd(OAc)_2$, Na_2CO_3, DMF, reflux; iii, NaH, MsCl, THF, rt; iv, $PdCl_2(PPh_3)_2$, $(SnBu_3)_2$, Li_2CO_3, Et_4NI, toluene (DMF), reflux.

3-Bromo-2-(2,2-dimethylpropanoylamino)pyridine; typical procedure for *ortho*-directed lithiation-bromination reaction of (2,2-dimethylpropanoylamino)pyridine

n-BuLi (1.94 ml, 2.62 mmol) was slowly added to a solution of 2-(2,2-dimethylpropanoylamino)pyridine (186.2 mg, 1.04 mmol) and TMEDA (0.39 ml, 2.62 mmol) in THF (5 ml) at −70 °C. The resulting solution was stirred at −70 °C for 15 min and at −10 °C for 2 h. Then the mixture was cooled to −70 °C, and 1,2-dibromoethane (0.23 ml, 2.62 mmol) was added. The resulting solution was stirred at −70 °C for 15 min and at −10 °C for 2 h. After evaporation of the THF, the residue was taken up into Et_2O, and the Et_2O phase was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica gel column chromatography using n-hexane–AcOEt (1:1) as eluent. The product was recrystallized from Et_2O–n-hexane to give 3-bromo-2-(2,2-dimethylpropanoylamino)pyridine as needles (132.6 mg, 50%), mp 140–141 °C (Found: C, 46.73; H, 5.04; Br, 31.18; N, 11.14. $C_{10}H_{13}BrN_2O$ requires C, 46.71; H, 5.10; Br, 31.08; N, 10.89%); ν_{max}(KBr)/cm^{-1} 3290 and 1650; δ_H 1.37 (9 H, s), 6.99 (1 H, dd, *J* 4.67, 7.97), 7.89 (1 H, dd, *J* 1.64, 7.97), 8.05 (1 H, br s), 8.46 (1 H, dd, *J* 1.37, 4.67); *m*/*z* 256 (M^+) (Found: M^+, 256.0209. Calc. for $C_{10}H_{13}{}^{79}BrN_2O$: *M*, 256.0211).

4-Bromo-3-(2,2-dimethylpropanoylamino)pyridine. According to the typical procedure, 4-bromo-3-(2,2-dimethylpropanoylamino)pyridine was obtained from the reaction using 3-(2,2-dimethylpropanoylamino)pyridine (340.1 mg, 1.91 mmol). Recrystallization from i-Pr_2O–n-hexane gave needles (204.2 mg, 45%), mp 98–99 °C (Found: C, 46.82; H, 5.09; Br, 30.84; N, 10.95%); ν_{max}(KBr)/cm^{-1} 3410 and 1705; δ_H 1.37 (9 H, s), 7.50 (1 H, d, *J* 5.22), 7.84 (1 H, br s), 8.18 (1 H, d, *J* 5.22), 9.54 (1 H, s); *m*/*z* 256 (M^+) (Found: M^+, 256.0250).

3-Bromo-4-(2,2-dimethylpropanoylamino)pyridine. According to the typical procedure, 3-bromo-4-(2,2-dimethylpropanoylamino)pyridine was obtained from the reaction using 4-(2,2-dimethylpropanoylamino)pyridine (1.38 g, 7.75 mmol). Recrystallization from i-Pr_2O–n-hexane gave prisms (1.64 g, 83%), mp 70–72 °C (Found: C, 46.51; H, 5.15; Br, 30.99; N, 10.70. $C_{10}H_{13}BrN_2O$ requires C, 46.71; H, 5.10; Br, 31.08; N, 10.89%); ν_{max}(KBr)/cm^{-1} 3275 and 1660; δ_H 1.36 (9 H, s), 8.17 (1 H, br s), 8.42 (1 H, d, *J* 0.82), 8.64 (1 H, s); *m*/*z* 256 (M^+) (Found: M^+, 256.0246. Calc. for $C_{11}H_9{}^{79}BrN_2O$: *M*, 256.0211).

2-Amino-3-bromopyridine 3a; typical procedure for alkaline hydrolysis reaction of *o*-bromo-(2,2-dimethylpropanoylamino)pyridine

A mixture of 3-bromo-2-(2,2-dimethylpropanoylamino)pyridine (8.35 g, 32.7 mmol) and 3 M KOH (15 ml) in MeOH (35 ml) was refluxed for 4 h. After removal of the solvent, the residue was diluted with Et_2O and the Et_2O phase was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica gel column chromatography using n-hexane–AcOEt (1:1) as eluent. The product was recrystallized from Et_2O–n-hexane to give needles (2.78 mg, 95%), mp 64–65 °C (Found: C, 34.78; H, 3.11; Br, 45.90; N, 16.34. $C_5H_5BrN_2$ requires C, 34.71; H, 2.91; Br, 46.18; N, 16.19%); ν_{max}(KBr)/cm^{-1} 3425; δ_H 4.92 (2 H, br s), 6.53–6.58 (1 H, m), 7.66 (1 H, dd, *J* 1.37, 6.59), 8.02 (1 H, dd, *J* 1.37, 4.95); *m*/*z* 172 (M^+) (Found: M^+, 171.9623. Calc. for $C_5H_5{}^{79}BrN_2$: *M*, 171.9636).

3-Amino-4-bromopyridine 3b. According to the typical procedure, **3b** was obtained from the reaction using 4-bromo-3-(2,2-dimethylpropanoylamino)pyridine (1.66 g, 6.5 mmol), as an oil (848.6 mg, 76%); bp 46–49 °C/3 mmHg; ν_{max}(neat)/cm^{-1} 3448; δ_H 4.14 (2 H, br s), 7.35 (1 H, dd, *J* 1.37, 4.95), 7.81 (1 H, d, *J* 4.67), 8.12 (1 H, s); *m*/*z* 172 (M^+) (Found: M^+, 171.9628).

4-Amino-3-bromopyridine 3c. According to the typical procedure, **3c** was obtained from the reaction 3-bromo-4-(2,2-dimethylpropanoylamino)pyridine (1.85 g, 7.25 mmol). Recrystallization from Et_2O–n-hexane gave needles (1.21 g, 97%), mp 70–71 °C (Found: C, 34.78; H, 3.14; Br, 45.98; N, 16.41%); ν_{max}(KBr)/cm^{-1} 3365; δ_H 4.65 (1 H, br s,), 6.61 (2 H, d, *J* 5.49), 8.12 (1 H, d, *J* 5.49), 8.41 (1 H, s); *m*/*z* 172 (M^+) (Found: M^+, 171.9641).

2-(2-Bromoanilino)pyridine 4a; typical procedure for the palladium-catalyzed reaction of iodobenzenes with arylamines

A mixture of 2-aminopyridine **2a** (343.6 mg, 3.65 mmol), 2-bromoiodobenzene **1a** (0.56 ml, 4.38 mmol), *t*-BuONa (475.7 mg, 5.11 mmol), $Pd_2(dba)_3$† (174.2 mg, 0.19 mmol), and DPPF‡ (204.9 mg, 0.37 mmol) in toluene (18 ml) was stirred at 100 °C for 14 h. After cooling, the mixture was diluted with Et_2O and filtered through a Celite® pad. The filtrate was evaporated, and purified by silica gel column chromatography using n-hexane–AcOEt (7:3) as eluent to give a pale yellow oil (853.9 mg, 94%); bp 140–143 °C/3 mmHg; ν_{max}(neat)/cm^{-1} 3410; δ_H 6.09 (1 H, br s), 6.98–6.84 (1 H, m), 7.16–7.27 (3 H, m), 7.45–7.49 (1 H, m), 7.55 (1 H, dd, *J* 1.10, 7.97), 8.27 (1 H, dd, *J* 1.10, 4.67), 8.47 (1 H, d, *J* 2.47); *m*/*z* 248 (M^+) (Found: M^+, 247.9940. Calc. for $C_{11}H_9{}^{79}BrN_2$: *M*, 247.9949).

4-(2-Bromoanilino)pyridine 4b. According to the typical procedure, **4b** was obtained from the reaction using 4-aminopyridine **2b** (222.1 mg, 2.36 mmol). Recrystallization from i-Pr_2O–n-hexane gave needles (555.9 mg, 96%), mp 94–95 °C (Found: C, 53.06; H, 3.62; Br, 32.07; N, 11.14. $C_{11}H_9BrN_2$ requires C, 53.04; H, 3.64; Br, 32.08; N, 11.25%); ν_{max}(KBr)/cm^{-1} 3207; δ_H 6.23 (1 H, br s), 6.89 (2 H, d, *J* 6.32), 6.98 (1 H,

† dba = dibenzylideneacetone.
‡ DPPF = 1,1′-bis(diphenylphosphino)ferrocine.

dt, *J* 1.37, 7.97), 7.31 (1 H, dt, *J* 1.37, 7.97), 7.46 (1 H, dd, *J* 1.37, 7.97), 7.62 (1 H, dd, *J* 1.37, 7.97), 8.36 (2 H, d, *J* 6.32); *m*/*z* 248 (M^+) (Found: M^+, 247.9935).

3-(2-Bromoanilino)pyridine 4c. According to the typical procedure, **4c** was obtained from the reaction using 3-aminopyridine **2c** (95.8 mg, 1.02 mmol), as a pale yellow oil (222.4 mg, 90%), bp 150–153 °C/3 mmHg; ν_{max}(neat)/cm^{-1} 3380; δ_H 6.07 (1 H, br s), 6.98–6.84 (1 H, m), 7.16–7.27 (3 H, m), 7.45–7.49 (1 H, m), 7.55 (1 H, dd, *J* 1.10, 7.97), 8.27 (1 H, dd, *J* 1.10, 4.67), 8.47 (1 H, d, *J* 2.75); *m*/*z* 248 (M^+) (Found: M^+, 247.9941).

2-Anilino-3-bromopyridine 5a. According to the typical procedure, **5a** was obtained from the reaction for 17 h using 2-amino-3-bromopyridine **3a** (638.0 mg, 3.68 mmol) and iodobenzene (0.90 ml, 4.43 mmol), as a pale yellow oil (817.4 mg, 90%), bp 153–156 °C/3 mmHg (Found: C, 52.98; H, 3.86; Br, 31.77; N, 11.13%); ν_{max}(neat)/cm^{-1} 3400; δ_H 6.63 (1 H, dd, *J* 4.95, 7.69), 7.01 (1 H, br s), 7.03–7.13 (1 H, m), 7.32–7.37 (2 H, m), 7.62 (2 H, d, *J* 7.69), 7.73 (1 H, dd, *J* 1.65, 7.69), 8.15 (1 H, dd, *J* 1.65, 4.67); *m*/*z* 248 (M^+) (Found: M^+, 247.9949).

3-Anilino-4-bromopyridine 5b. According to the typical procedure, **5b** was obtained from the reaction for 17 h using 3-amino-4-bromopyridine **3b** (824.3 mg, 4.79 mmol) and iodobenzene (0.64 ml, 5.75 mmol). Recrystallization from i-Pr_2O–n-hexane gave needles (628.3 mg, 53%), mp 109–110 °C (Found: C, 53.04; H, 3.69; Br, 32.08; N, 11.18%); ν_{max}(KBr)/cm^{-1} 3220; δ_H 5.96 (1 H, br s), 7.11 (1 H, t, *J* 7.42), 7.19 (1 H, d, *J* 7.69), 7.36 (1 H, dt, *J* 1.92, 7.42), 7.46 (1 H, d, *J* 5.22), 7.93 (1 H, d, *J* 4.95), 8.51 (1 H, s); *m*/*z* 248 (M^+) (Found: M^+, 247.9928).

4-Anilino-3-bromopyridine 5c. According to the typical procedure, **5c** was obtained from the reaction for 17 h using 4-amino-3-bromopyridine **3c** (342.7 mg, 1.99 mmol) and iodobenzene (0.27 ml, 2.39 mmol). Recrystallization from i-Pr_2O–n-hexane gave plates (436.4 mg, 88%), mp 66–68 °C (Found: C, 53.09; H, 3.66; Br, 31.99; N, 11.08%); ν_{max}(KBr)/cm^{-1} 3380; δ_H 6.50 (1 H, br s), 6.92 (1 H, d, *J* 5.77), 7.20–7.27 (3 H, m), 7.39–7.44 (2 H, m), 8.14 (1 H, d, *J* 5.49), 8.49 (1 H, s); *m*/*z* 248 (M^+) (Found: M^+, 247.9919).

3-Anilino-2-bromopyridine 5d. According to the typical procedure, **5d** was obtained from the reaction for 17 h using 3-amino-2-bromopyridine **3d** (142.9 mg, 0.90 mmol) and iodobenzene (0.12 ml, 1.08 mmol). Recrystallization from i-Pr_2O–n-hexane gave needles (142.5 mg, 64%), mp 85–86 °C (Found: C, 53.03; H, 3.83; Br, 32.13; N, 11.44. $C_{11}H_9BrN_2$ requires C, 53.04; H, 3.64; Br, 32.08; N, 11.25%); ν_{max}(KBr)/cm^{-1} 3400; δ_H 6.16 (1 H, br s), 7.06–7.18 (4 H, m), 7.30–7.40 (2 H, m), 7.43 (1 H, dd, *J* 1.65, 7.97), 7.85 (1 H, dd, *J* 1.65, 4.67); *m*/*z* 248 (M^+) (Found: M^+, 247.9949).

3-Bromo-2-(2-bromoanilino)pyridine 6a. According to the typical procedure, **6a** was obtained from the reaction for 18 h using 2-amino-3-bromopyridine **3a** (188.7 mg, 1.10 mmol) and 2-bromoiodobenzene **1a** (0.17 ml, 1.32 mmol). Recrystallization from n-hexane gave prisms (333.8 mg, 93%), mp 73–74 °C (Found: C, 40.12; H, 2.49; Br, 48.70; N, 8.48. $C_{11}H_8Br_2N_2$ requires C, 40.28; H, 2.46; Br, 48.72; N, 8.54%); ν_{max}(KBr)/cm^{-1} 3355; δ_H 6.71 (1 H, dd, *J* 4.95, 7.69), 6.90 (1 H, dt, *J* 1.37, 7.69), 7.33 (1 H, dt, *J* 1.37, 8.24), 7.57 (1 H, dd, *J* 1.37, 7.96), 7.73 (1 H, br s), 7.80 (1 H, dd, *J* 1.65, 7.96), 8.19 (1 H, dd, *J* 1.65, 4.65), 8.59 (1 H, dd, *J* 1.65, 8.24); *m*/*z* 326 (M^+) (Found: M^+, 325.9032. Calc. for $C_{11}H_8{}^{79}Br_2N_2$: *M*, 325.9055).

4-Bromo-3-(2-bromoanilino)pyridine 6b. According to the typical procedure, **6b** was obtained from the reaction for 18 h using 3-amino-4-bromopyridine **3b** (909.2 mg, 5.29 mmol) and 2-bromoiodobenzene **1a** (0.81 ml, 6.34 mmol). Recrystallization from n-hexane gave needles (1.49 g, 86%), mp 89–91 °C (Found: C, 40.51; H, 2.59; Br, 48.69; N, 8.52%); ν_{max}(KBr)/cm^{-1} 3380; δ_H 6.30 (1 H, br s), 6.89–6.94 (1 H, m), 7.23–7.33 (2 H, m), 7.52 (1 H, d, *J* 5.22), 7.62 (1 H, dd, *J* 1.10, 7.96), 8.02 (1 H, d, *J* 5.22), 8.54 (1 H, s); *m*/*z* 326 (M^+) (Found: M^+, 325.9009).

3-Bromo-4-(2-bromoanilino)pyridine 6c. According to the typical procedure, **6c** was obtained from the reaction for 18 h using 4-amino-3-bromopyridine **3c** (946.8 mg, 5.50 mmol) and 2-bromoiodobenzene **1a** (0.85 ml, 6.61 mmol). Recrystallization from $CHCl_3$–n-hexane gave needles (1.67 g, 90%), mp 125–127 °C (Found: C, 40.38; H, 2.54; Br, 48.81; N, 8.47%); ν_{max}(KBr)/cm^{-1} 3380; δ_H 6.74 (1 H, br s), 6.93 (1 H, d, *J* 5.77), 7.08 (1 H, dt, *J* 1.65, 7.69), 7.36 (1 H, dt, *J* 1.37, 8.24), 7.45 (1 H, dd, *J* 1.65, 8.24), 7.68 (1 H, dd, *J* 1.37, 8.24), 8.19 (1 H, d, *J* 5.77), 8.55 (1 H, s); *m*/*z* 326 (M^+) (Found: M^+, 325.9034).

2-Bromo-3-(2-bromoanilino)pyridine 6d. According to the typical procedure, **6d** was obtained from the reaction for 18 h using 3-amino-2-bromopyridine **3d** (554.8 mg, 3.23 mmol) and 2-bromoiodobenzene **1a** (0.50 ml, 3.87 mmol). Recrystallization from n-hexane gave needles (751.7 mg, 71%), mp 49–51 °C (Found: C, 40.45; H, 2.64; Br, 48.67; N, 8.52%); ν_{max}(KBr)/cm^{-1} 3375; δ_H 6.49 (1 H, br s), 6.92–6.98 (1 H, m), 7.15 (1 H, dd, *J* 4.67, 8.24), 7.27–7.32 (2 H, m), 7.47 (1 H, dd, *J* 1.65, 7.96), 7.63 (1 H, d, *J* 8.79), 7.94 (1 H, dd, *J* 1.37, 4.67); *m*/*z* 326 (M^+) (Found: M^+, 325.9019).

2-Bromodiphenylamine 12a. According to the typical procedure, **12a** was obtained from the reaction for 12 h using aniline **11a** (94.9 mg, 1.02 mmol) and **1a** (0.16 ml, 1.22 mmol), as a pale yellow oil (116.2 mg, 46%), bp 138–141 °C/3 mmHg; ν_{max}(neat)/cm^{-1} 3390; δ_H 6.08 (1 H, br s), 6.73 (1 H, dt, *J* 1.65, 7.96), 7.01–7.07 (1 H, m), 7.13–7.19 (3 H, m), 7.25 (1 H, dd, *J* 1.37, 5.77), 7.29–7.35 (2 H, m), 7.52 (1 H, dd, *J* 1.65, 7.96); *m*/*z* 247 (M^+) (Found: M^+, 246.9984. Calc. for $C_{12}H_{10}{}^{79}BrN$: *M*, 246.9996).

2,2′-Dibromodiphenylamine 12b. According to the typical procedure, **12b** was obtained from the reaction for 12 h using 2-bromoaniline **11b** (821.9 mg, 4.78 mmol) and **1a** (0.74 ml, 5.73 mmol), as an oil (1.50 g, 96%), bp 154–158 °C/3 mmHg; ν_{max}(KBr)/cm^{-1} 3370; δ_H 6.44 (1 H, br s), 6.84 (2 H, dt, *J* 1.65, 7.96), 7.22 (2 H, dd, *J* 1.37, 8.24), 7.29 (2 H, dt, *J* 1.65, 8.24), 7.58 (2 H, dd, *J* 1.37, 7.96); *m*/*z* 325 (M^+) (Found: M^+, 324.9092. Calc. for $C_{12}H_9{}^{79}Br_2N$: *M*, 324.9102).

9*H*-Pyrido[2,3-*b*]indole or α-carboline 8a; typical procedure for the palladium-catalyzed reaction of *ortho*-anilinobromoarenes

A mixture of **5a** (204.5 mg, 0.82 mmol), $Pd(OAc)_2$ (18.5 mg, 0.08 mmol), and Na_2CO_3 (143.1 mg, 1.15 mmol) in DMF (7 ml) was refluxed for 67 h. After cooling, the mixture was diluted with AcOEt and filtered through a Celite® pad. The filtrate was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica gel column chromatography using n-hexane–AcOEt (1 : 1) as eluent. The product was recrystallized from toluene to give needles (43.3 mg, 31%), mp 210–211 °C (lit.,[4a] 212 °C); ν_{max}(KBr)/cm^{-1} 3400; δ_H($CDCl_3$–d_6-DMSO) 7.19 (1 H, dd, *J* 4.95, 7.49), 7.25–7.30 (1 H, m), 7.45–7.55 (2 H, m), 8.07 (1 H, d, *J* 7.69), 8.34 (1 H, dd, *J* 1.65, 7.69), 8.47 (1 H, d, *J* 7.69).

9*H*-Pyrido[3,4-*b*]indole or β-carboline 8b. According to the typical procedure, **8b** was obtained from the reaction using **5b** (132.5 mg, 0.53 mmol). Recrystallization from toluene gave needles (54.1 mg, 61%), mp 199–200 °C (lit.,[4a] mp 198–200 °C); ν_{max}(KBr)/cm^{-1} 3400; δ_H($CDCl_3$–d_6-DMSO) 7.19 (1 H, dd, *J* 2.74, 5.22), 7.42–7.47 (2 H, m), 7.88 (1 H, d, *J* 5.22), 8.05 (1 H, d, *J* 7.69), 8.34 (1 H, dd, *J* 5.22), 8.84 (1 H, s), 10.14 (1 H, br s).

5*H*-Pyrido[4,3-*b*]indole or γ-carboline 8c. According to the typical procedure, **8c** was obtained from the reaction using **5c** (151.2 mg, 0.61 mmol). Yield 48 mg (47%).

According to the typical procedure, **8c** was obtained from the reaction after 10 h using **4b** (257.1 mg, 1.04 mmol). Yield 123.0 mg (70%). Recrystallization from toluene gave needles, mp 216–218 °C (lit.,[4a] 218 °C); ν_{max}(KBr)/cm^{-1} 3400; δ_H(CDCl$_3$–d_6-DMSO) 6.98 (1 H, dt, *J* 1.37, 7.69), 7.08–7.24 (3 H, m), 7.82 (1 H, d, *J* 7.69), 8.16 (1 H, d, *J* 8.24), 8.99 (1 H, s), 10.54 (1 H, br s).

5*H*-Pyrido[3,2-*b*]indole or δ-carboline 8d. According to the typical procedure, **8d** was obtained from the reaction using **5d** (142.5 mg, 0.57 mmol). Yield 49.0 mg (51%).

According to the typical procedure, **8c** was obtained from the reaction after 14 h using **4b** (117.2 mg, 0.47 mmol). Yield 40.1 mg (51%). Recrystallization from toluene gave needles, mp 205–207 °C (lit.,[4a] 206 °C); ν_{max}(KBr)/cm^{-1} 3400; δ_H(CDCl$_3$–d_6-DMSO) 6.97–7.07 (2 H, m), 7.19–7.25 (2 H, m), 7.52 (1 H, dd, *J* 1.37, 8.24), 8.05 (1 H, d, *J* 7.69), 8.24 (1 H, d, *J* 4.67), 10.29 (1 H, br s).

Pyrido[1,2-*a*]benzimidazole 10. According to the typical procedure, **10** was obtained from the reaction using **4a** (672.1 mg, 2.71 mmol). Recrystallization from acetone–n-hexane gave needles (269.8 mg, 59%), mp 179–182 °C (lit.,[11] 180 °C); δ_H 6.87 (1 H, t, *J* 6.87), 7.36–7.47 (2 H, m), 7.55 (1 H, dt, *J* 1.10, 8.24), 7.71 (1 H, d, *J* 9.34), 7.91 (1 H, d, *J* 8.24), 7.95 (1 H, d, *J* 8.24), 8.47 (1 H, d, *J* 6.87); *m*/*z* 168 (M$^+$) (Found: M$^+$, 168.0683. Calc. for $C_{11}H_8N_2$: *M*, 168.0687).

Carbazole 14a. According to the typical procedure, **14** was obtained from the reaction for 15 h using **12a** (219.1 mg, 0.89 mmol). Recrystallization from acetone–n-hexane gave needles (60.5 mg, 41%), mp 242–247 °C (lit.,[12] 246 °C); ν_{max}(KBr)/$^{-1}$ 3415; δ_H(CDCl$_3$–d_6-DMSO) 7.22 (2 H, dt, *J* 1.37, 7.69), 7.38–7.44 (4 H, m), 8.08 (2 H, d, *J* 7.69), 9.03 (1 H, br s).

3-Bromo-2-[2-bromo-*N*-(methylsulfonyl)anilino]pyridine 7a; typical procedure for the preparation of 2,2′-dibromo-*N*-(methylsulfonyl)diarylamines

A THF (5 ml) solution of **6a** (353.4 mg, 1.08 mmol) was added dropwise to a THF (5 ml) suspension of 60% NaH (130.1 mg, 3.25 mmol), and the mixture was stirred at room temperature (rt) for 1 h. To this mixture was added methanesulfonyl chloride (0.17 ml, 2.16 mmol), and the whole mixture was stirred at rt for 4 h. After evaporation of the THF, the residue was taken up into AcOEt. The AcOEt phase was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica gel column chromatography with n-hexane–AcOEt (4:1) as eluent. The product was recrystallized from acetone–n-hexane to give needles (340.6 mg, 78%), mp 120–122 °C (Found: C, 35.55; H, 2.50; Br, 39.54; N, 6.83; S, 7.87. $C_{12}H_{10}Br_2N_2O_2S$ requires C, 35.49; H, 2.48; Br, 39.35; N, 6.90; S, 7.89%); ν_{max}(KBr)/cm^{-1} 1350 and 1150; δ_H 3.55 (3 H, s), 7.09 (1 H, dd, *J* 4.95, 7.69), 7.24 (1 H, dt, *J* 1.37, 7.69), 7.40 (1 H, dt, *J* 1.37, 8.29), 7.58 (1 H, dd, *J* 1.37, 7.96), 7.88 (1 H, dd, *J* 1.65, 7.96), 7.93 (1 H, dd, *J* 1.65, 8.24), 8.47 (1 H, dd, *J* 1.65, 4.65); *m*/*z* 404 (M$^+$) (Found: M$^+$, 403.8830. Calc. for $C_{12}H_{10}{}^{79}Br_2N_2O_2S$: *M*, 403.8830).

4-Bromo-3-[2-bromo-*N*-(methylsulfonyl)anilino]pyridine 7b. According to the typical procedure, **7b** was obtained from the reaction using **6b** (408.3 mg, 1.25 mmol). Recrystallization from acetone–n-hexane gave needles (420.8 mg, 83%), mp 159–160 °C (Found: C, 35.58; H, 2.52; Br, 39.44; N, 6.80; S, 7.82%); ν_{max}(KBr)/cm^{-1} 1350 and 1130; δ_H 3.31 (3 H, s), 7.27 (1 H, dt, *J* 1.65, 8.24), 7.43 (1 H, dt, *J* 1.65, 8.24), 7.59 (1 H, d, *J* 5.22), 7.65 (1 H, dd, *J* 1.65, 7.96), 8.16 (1 H, dd, *J* 1.65, 8.24), 8.32 (1 H, d, *J* 5.22), 9.14 (1 H, s); *m*/*z* 404 (M$^+$) (Found: M$^+$, 403.8832).

3-Bromo-4-[2-bromo-*N*-(methylsulfonyl)anilino]pyridine 7c. According to the typical procedure, **7c** was obtained from the reaction using **6c** (570.4 mg, 1.75 mmol). Recrystallization from MeOH gave needles (579.7 mg, 82%), mp 199–201 °C (Found: C, 35.51; H, 2.54; Br, 39.60; N, 6.88; S, 7.92%); ν_{max}(KBr)/cm^{-1} 1350 and 1120; δ_H 3.32 (3 H, s), 7.29 (1 H, dt, *J* 1.65, 7.69), 7.45 (1 H, dt, *J* 1.65, 7.96), 7.64–7.69 (2 H, m), 8.06 (1 H, dd, *J* 1.65, 8.24), 8.53 (1 H, d, *J* 5.94), 8.79 (1 H, s); *m*/*z* 404 (M$^+$) (Found: M$^+$, 403.8826).

2-Bromo-3-[2-bromo-*N*-(methylsulfonyl)anilino]pyridine 7d. According to the typical procedure, **7d** was obtained from the reaction using **6d** (275.4 mg, 0.85 mmol). Recrystallization from acetone–n-hexane gave needles (327.5 mg, 95%), mp 142–143 °C (Found: C, 35.57; H, 2.49; Br, 39.46; N, 6.91; S, 7.86%); ν_{max}(KBr)/cm^{-1} 1350 and 1120; δ_H 3.31 (3 H, s), 7.23–7.28 (1 H, m), 7.36–7.46 (2 H, m), 7.65 (1 H, dd, *J* 1.65, 7.96), 8.09 (1 H, dd, *J* 1.37, 8.24), 8.35 (1 H, dd, *J* 1.65, 4.77), 8.42 (1 H, dd, *J* 1.37, 7.96); *m*/*z* 404 (M$^+$) (Found: M$^+$, 403.8839).

2,2′-Dibromo-*N*-(methylsulfonyl)diphenylamine 13. According to the typical procedure, **13** was obtained from the reaction using **12b** (670.1 mg, 2.05 mmol). Recrystallization from acetone–n-hexane gave needles (692.7 mg, 83%), mp 163–165 °C (Found: C, 38.49; H, 2.81; Br, 39.66; N, 3.52; S, 7.87. $C_{13}H_{11}Br_2NO_2S$ requires C, 38.54; H, 2.74; Br, 39.45; N, 3.46; S, 7.91%); ν_{max}(KBr)/cm^{-1} 3220; δ_H 3.30 (3 H, s), 7.21 (2 H, dt, *J* 1.65, 7.96), 7.38 (2 H, dt, *J* 1.65, 7.96), 7.65 (2 H, dd, *J* 1.65, 7.96), 8.08 (2 H, dd, *J* 1.37, 7.96); *m*/*z* 403 (M$^+$) (Found: M$^+$, 402.8901. Calc. for $C_{13}H_{11}{}^{79}Br_2NO_2S$: *M*, 402.8878).

9-Methylsulfonyl-α-carboline 9a; typical procedure for the palladium-catalyzed cyclization reaction of *ortho*,*ortho*′-dibromoarylamines 7a–d, 13

A mixture of **7a** (131.9 mg, 0.32 mmol), $(Bu_3Sn)_2$ (0.19 ml, 0.38 mmol), Et_4NI (115.2 mg, 0.45 mmol), Li_2CO_3 (33.1 mg, 0.45 mmol), $Pd(PPh_3)_2Cl_2$ (22.8 mg, 0.03 mol), and toluene (5 ml) was refluxed for 6 h. After cooling, the mixture was diluted with Et_2O and filtered through a Celite® pad. The filtrate was evaporated, and the residue was purified by silica gel column chromatography using n-hexane–AcOEt (7:3) as eluent. The product was recrystallized from acetone–n-hexane to give needles (71.4 mg, 91%), mp 109–110 °C (Found: C, 58.49; H, 4.10; N, 11.40; S, 13.01. $C_{12}H_{10}N_2O_2S$ requires C, 58.52; H, 4.09; N, 11.37; S, 13.02%); ν_{max}(KBr)/cm^{-1} 1355 and 1120; δ_H 3.61 (3 H, s), 7.38 (1 H, dd, *J* 4.95, 7.69), 7.43 (1 H, dt, *J* 1.10, 7.42), 7.55 (1 H, dt, *J* 1.37, 7.42), 8.01 (1 H, d, *J* 7.69), 8.32 (1 H, dd, *J* 1.65, 7.69), 8.33 (1 H, d, *J* 8.52), 8.61 (1 H, dd, *J* 1.65, 4.94); *m*/*z* 246 (M$^+$) (Found: M$^+$, 246.0436. Calc. for $C_{12}H_{10}N_2O_2S$: *M*, 246.0462).

9-Methylsulfonyl-β-carboline 9b. According to the typical procedure, **9b** was obtained from the reaction using **7b** (131.9 mg, 0.33 mmol) and toluene–DMF (10:1; 5 ml) as solvent. Recrystallization from acetone–n-hexane gave needles (51.5 mg, 64%), mp 163–165 °C (Found: C, 58.48; H, 3.82; N, 11.35; S, 13.04%); ν_{max}(KBr)/cm^{-1} 1355 and 1115; δ_H 3.08 (3 H, s), 7.51 (1 H, dt, *J* 1.10, 9.96), 7.68 (1 H, dt, *J* 1.37, 8.24), 7.93 (1 H, d, *J* 5.22), 8.11 (1 H, d, *J* 7.96), 8.21 (1 H, d, *J* 8.24), 8.69 (1 H, d, *J* 5.22), 9.50 (1 H, s); *m*/*z* 246 (M$^+$) (Found: M$^+$, 246.0450).

5-Methylsulfonyl-γ-carboline 9c. According to the typical procedure, **9c** was obtained from the reaction using **7c** (464.6 mg, 1.15 mmol) and toluene–DMF (10:1; 5 ml) as solvent. Recrystallization from $CHCl_3$–n-hexane gave needles (210.3 mg, 74%), mp 165–166 °C (Found: C, 58.19; H, 3.94; N, 11.29;

S, 13.11%); ν_{max}(KBr)/cm^{-1} 1350 and 1125; δ_H 3.12 (3 H, s), 7.64–7.71 (2 H, m), 8.06 (1 H, d, *J* 6.04), 8.12 (1 H, d, *J* 7.42), 8.17 (1 H, d, *J* 8.24), 8.68 (1 H, d, *J* 6.04), 9.33 (1 H, s); *m*/*z* 246 (M^+). (Found: M^+, 246.0442).

5-Methylsulfonyl-δ-carboline 9d. According to the typical procedure, **9d** was obtained from the reaction using **7d** (237.9 mg, 0.58 mmol). Recrystallization from acetone–n-hexane gave needles (119.3 mg, 84%), mp 153–154 °C; ν_{max}(KBr)/cm^{-1} 1358 and 1115 (Found: C, 58.55; H, 4.12; N, 11.29; S, 13.21%); δ_H 3.03 (3 H, s), 7.43 (1 H, dd, *J* 4.67, 8.52), 7.51–7.56 (1 H, m), 7.64 (1 H, dt, *J* 1.37, 8.24), 8.19 (1 H, d, *J* 8.52), 8.35 (1 H, d, *J* 7.69), 8.45 (1 H, dd, *J* 1.37, 8.52), 8.71 (1 H, dd, *J* 1.37, 4.95); *m*/*z* 246 (Found: M^+, 246.0465).

9-(Methylsulfonyl)carbazole 14b. According to the typical procedure, **14b** was obtained from the reaction using **13** (137.2 mg, 0.34 mmol). Recrystallization from n-hexane gave needles (39.2 mg, 47%), mp 108–109 °C (Found: C, 63.70; H, 4.49; N, 5.74; S, 13.10. $C_{13}H_{11}NO_2S$ requires C, 63.66; H, 4.52; N, 5.71; S, 13.07%); ν_{max}(KBr)/cm^{-1} 1350 and 1120; δ_H 2.99 (3 H, s), 7.41–7.54 (4 H, m), 8.03 (2 H, d, *J* 7.69), 8.18 (2 H, d, *J* 8.24); *m*/*z* 245 (M^+) (Found: M^+, 245.0506. Calc. for $C_{13}H_{11}NO_2S$: *M*, 245.0510).

References

1 (*a*) J. V. Greenhill, in *Comprehensive Heterocyclic Chemistry*, eds. A. R. Katritzky and C. R. Rees, Pergamon Press, Oxford, 1984, vol. 4, p. 497; (*b*) R. A. Abramovitch and I. D. Spenser, *Adv. Heterocycl. Chem.*, 1964, **3**, 79.

2 (*a*) B. Witkop, *J. Am. Chem. Soc.*, 1953, **75**, 3361; (*b*) A. Molina, J. J. Vaquero, J. L. Garcia-Navio and J. Alvarez-Builla, *Tetrahedron Lett.*, 1993, **34**, 2673; (*c*) A. Molina, J. J. Vaquero, J. L. Garcia-Navio, J. Alvarez-Builla, B. de Pascual-Teresa, F. Gago, M. M. Rodrigo and M. Ballesteros, *J. Org. Chem.*, 1996, **61**, 5587; (*d*) O. Bremer, *Justus Liebigs Ann. Chem.*, 1934, **514**, 279; (*e*) R. A. Abramovitch, D. H. Hey and R. D. Mulley, *J. Chem. Soc.*, 1954, 4263; (*f*) R. A. Abramovitch, *Can. J. Chem.*, 1960, **38**, 2273.

3 (*a*) P. A. S. Smith and J. H. Boyer, *J. Am. Chem. Soc.*, 1951, **73**, 2626; (*b*) R. A. Abramovitch, K. A. H. Adams and A. D. Notation, *Can. J. Chem.*, 1960, **38**, 2152; (*c*) P. J. Bunyan and J. I. G. Cadogan, *J. Chem. Soc.*, 1963, 42; (*d*) R. A. Abramovitch, *J. Chem. Soc.*, 1964, 2175; (*e*) T. Kametani, K. Ogasawara and T. Yamanaka, *J. Chem. Soc. C*, 1968, 1006.

4 P. Rocca, F. Marsais, A. Godard and G. Quéguiner, *Tetrahedron*, 1993, **49**, (*a*) 49; (*b*) 3325; (*c*) *Tetrahedron Lett.*, 1993, **34**, 7917; (*d*) *J. Heterocycl. Chem.*, 1995, **32**, 1171.

5 (*a*) A. S. Guram, R. A. Rennels and S. L. Buchwald, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1348; (*b*) J. F. Louie and J. F. Hartwig, *Tetrahedron Lett.*, 1995, **36**, 3609.

6 D. E. Ames and D. Bull, *Tetrahedron*, 1982, **38**, 383.

7 (*a*) T. R. Kelly, Q. Li and V. Bhushan, *Tetrahedron Lett.*, 1990, **31**, 161; (*b*) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508; (*c*) T. R. Bailey, *Tetrahedron Lett.*, 1986, **27**, 4407; (*d*) A. M. Echavarren and J. K. Stille, *J. Am. Chem. Soc.*, 1987, **109**, 5486.

8 (*a*) Y. Akita, A. Inoue, K. Yamamoto, A. Ohta, T. Kurihara and M. Shimizu, *Heterocycles*, 1985, **23**, 2327; (*b*) Y. Akita, Y. Itagaki, S. Takizawa and A. Ohta, *Chem. Pharm. Bull.*, 1989, **37**, 1477; (*c*) A. Aoyagi, A. Inoue, K. Koizumi, R. Hashimoto, K. Tokunaga, K. Gohma, J. Komatsu, K. Sekine, A. Miyafuji, J. Kunoh, R. Honma, Y. Akita and A. Ohta, *Heterocycles*, 1992, **33**, 257; (*d*) A. Ohta, Y. Akita, T. Ohkuwa, M. Chiba, R. Fukunaga, A. Miyafuji, T. Nakata and N. Tani, *Heterocycles*, 1990, **31**, 1951.

9 L. Estel, F. Linard, F. Marsais, A. Godard and G. Quéguiner, *J. Heterocycl. Chem.*, 1989, **26**, 105.

10 G. J. Fox, J. D. Hepworth and G. Halias, *J. Chem. Soc., Perkin Trans. 1*, 1973, 68.

11 C. Combet-Farnoux and M. Miocque, *J. Heterocycl. Chem.*, 1985, **22**, 369.

12 *The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, eds. C. J. Pouchert and J. Behnke, Aldrich Chemical Co. Ltd., New York, 1993, vol. 3, p. 160.

Paper 9/01088B