A practical approach to stereodefined cyclopropyl-substituted heteroarenes using a Suzuki-type reaction

Min-Liang Yao and Min-Zhi Deng*

Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Academia Sinica, 354 FengLin Lu, Shanghai 200032, China.
E-mail: dengmz@pub.sioc.ac.cn; Fax: +86 21 6416 6128

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In the presence of $Pd(PPh_3)_4$, NaBr and $KF \cdot 2H_2O$ the cross-coupling reaction of heteroaryl triflates with *trans*-cyclopropylboronic acids proceeds readily to give pure *trans*-cyclopropyl heteroarenes in moderate to good yields. The X-ray crystallography of compound **3g** and ^{1}H-NMR spectra of all products show that the configuration of the cyclopropyl group was retained during the reaction. Under the same reaction conditions, highly optically active cyclopropyl-substituted heteroarenes (up to 94% ee) were obtained by cross-coupling of heteroary/triflates with enantiomerically enriched cyclopropylboronic acids.

Cyclopropyl-substituted heteroaryl moieties are present in many biologically active natural products[1] and synthetic drugs,[2] so the stereodefined cyclopropyl unit is increasingly being incorporated into molecules for their well-defined three-dimensional structure.[3] Although the introduction of simple cyclopropyl groups into heteroarenes has been reported,[4] general methods for introducing substituted and stereocontrolled cyclopropyl groups into heteroarenes are still scarce. Recently, the preparation of heteroaryl derivatives using palladium-catalyzed protocols has attracted the interest of many chemists.[5] Among these protocols, the Suzuki-type reaction[6] is appealing, since boronic acids (or esters) are thermally stable and relatively unreactive to both air and water.

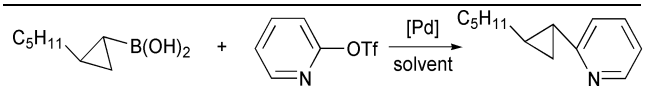
The success of cyclopropylboronic acids (or esters) in the cross-coupling reaction[7] demonstrated that they were useful reagents to prepare cyclopropyl-substituted compounds. In addition, enantiomerically enriched cyclopropylboronic acids (or esters) can be readily prepared by several methods.[8] So the Suzuki-type reaction between cyclopropylboronic acids and eletrophiles to prepare cyclopropyl-substituted heteroarenes is considered to be quite practical. Furthermore, by changing the substituent on the cyclopropylboronic acid component, the fat-solubility of the products can be easily adjusted. This modulation is always very important in pharmaceutical research.

The coupling reaction of heteroaryl bromides with cyclopropylboronic acids has been reported by our group,[9] considering that some heteroaryl bromides are difficult to prepare, the study of the corresponding reaction of hetroaryl triflates to make up for this drawback is necessary. Herein we wish to report the results.

Results and discussion

Initially, we examined the cross-coupling reaction of *trans*-2-pentylcyclopropylboronic acid with 2-pyridyl triflate to develop the optimum reaction conditions. As shown in Table 1, the solvent and base used affected the reaction greatly. Considering that ethereal solvents were frequently used in the cross-coupling reactions of triflates with organoboron compounds, dioxane and THF were initially tested. However, the expected reaction did not take place (entries 1, 2). Even when adding 1 equiv. NaBr, only a trace of desired product was detected (entry 3). When the reaction was conducted in the presence of a catalytic amount of $Pd(PPh_3)_4$, using toluene as the solvent and $K_3PO_4 \cdot 3H_2O$ as the base (entry 4), the anticipated 2-cyclopropyl-substituted pyridine product was obtained in 43% yield. If 1 equiv. NaBr was added, the yield increased to 74% (entry 5). But the yield decreased to 49% when using 2 M KOH as the base (entry 6), this can be rationalized by the partial decomposition of 2-pyridyl triflate by the strong base.[10] So we turned our attention towards the weakly basic $KF \cdot 2H_2O$ and found that the yield improved to 77% (entry 7). The addition of NaBr seemed to be necessary to make the reaction proceed readily (compare entry 4 with 5 and entry 7 with 8). Presumably the bromide ion converts the labile cationic palladium(II) species (A) to organopalladium(II)bromide (B), which favours the trans-

Table 1 Coupling of *trans*-pentylcyclopropylboronic acid with 2-pyridyl triflate[a]



Entry	Conditions	Yield[b]/%
1	1,4-Dioxane, $K_3PO_4 \cdot 3H_2O$, $Pd(PPh_3)_4$, 100 °C	0
2	THF, $K_3PO_4 \cdot 3H_2O$, $Pd(PPh_3)_4$, 70 °C	0
3	THF, $K_3PO_4 \cdot 3H_2O$, NaBr, $Pd(PPh_3)_4$, 70 °C	Trace
4	Toluene, $K_3PO_4 \cdot 3H_2O$, $Pd(PPh_3)_4$, 100 °C	43
5	Toluene, $K_3PO_4 \cdot 3H_2O$, NaBr, $Pd(PPh_3)_4$, 100 °C	74
6	Toluene, 2 M KOH, NaBr, $Pd(PPh_3)_4$, 100 °C	49
7	Toluene, $KF \cdot 2H_2O$, NaBr, $Pd(PPh_3)_4$, 100 °C	77
8	Toluene, $KF \cdot 2H_2O$, $Pd(PPh_3)_4$, 100 °C	51
9	Toluene, $KF \cdot 2H_2O$; NaBr, $Pd(PPh_3)_2Cl_2$, 100 °C	0

[a] Reactions were carried out for 22 h using 0.03 mmol of catalyst, 2-pyridyl triflate (1.0 mmol) and *trans*-2-pentylcyclopropylboronic acid (1.1 mmol) in 4 ml solvent. [b] Isolated yield based on 2-pyridyl triflate.

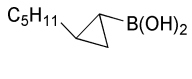
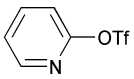
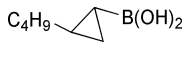
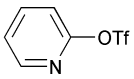
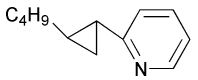
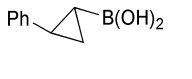
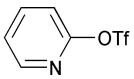
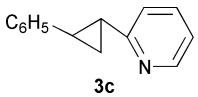
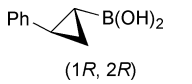
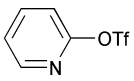
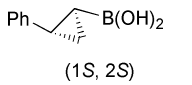
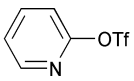
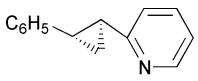
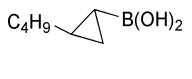
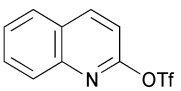
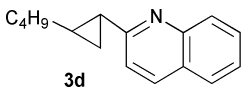
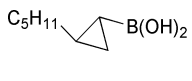
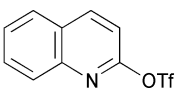
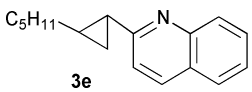
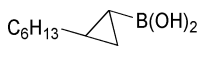
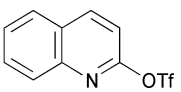
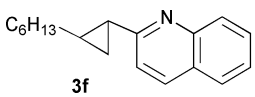
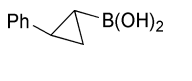
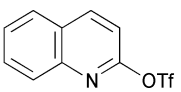
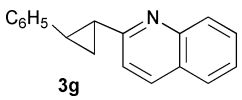
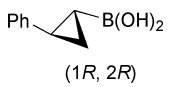
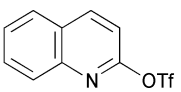
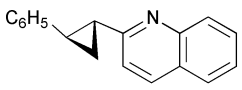
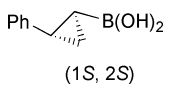
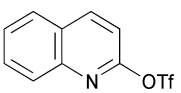
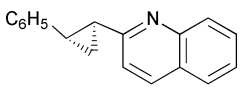
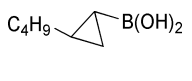
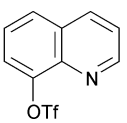
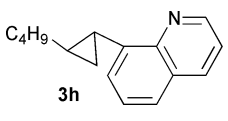
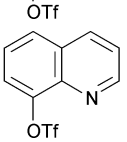
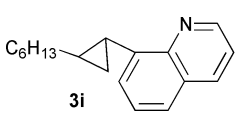
metallation reaction between (B) and cyclopropylboronic acids.

$$ArOTf \xrightarrow{Pd^0L_n} \underset{(A)}{ArPd^{II}OTf} \xrightarrow{Br^-} \underset{(B).}{ArPd^{II}Br}$$

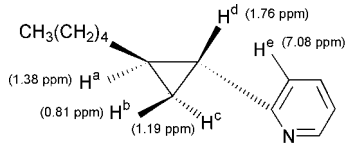
Considering that $Pd(PPh_3)_2Cl_2$ is air-stable and storable, we tried to use $Pd(PPh_3)_2Cl_2$ instead of $Pd(PPh_3)_4$, but the reaction failed (entry 9). Thus, the nonpolar solvent toluene seems to be more effective than ethereal solvents and the weakly basic $KF \cdot 2H_2O$ is superior to the strong base KOH; the addition of NaBr improved the conversion.

After having established the optimized coupling reaction conditions, the scope of the reaction was evaluated by investigating the coupling of various heteroaryl triflates and cyclo-

Table 2 Cross-coupling reactions of heteroaryl triflates with *trans*-2-substituted cyclopropylboronic acids[a]

Entry	Cyclopropylboronic acid (**1**)	Heteroaryl triflate (**2**)	Product (**3**)	Yield[b]/ %
1			 **3a**	77
2			 **3b**	73
3			 **3c**	71
4[c]	 (1*R*, 2*R*)		 **3c** (1*R*, 2*R*)	73
5[d]	 (1*S*, 2*S*)		 **3c** (1*S*, 2*S*)	72
6			 **3d**	79
7			 **3e**	85
8			 **3f**	67
9			 **3g**	75
10[e]	 (1*R*, 2*R*)		 **3g** (1*R*, 2*R*)	67
11[f]	 (1*S*, 2*S*)		 **3g** (1*S*, 2*S*)	71
12			 **3h**	73
13			 **3i**	72

[a] Reactions were carried out at 100 °C using 0.03 mmol of $Pd(PPh_3)_4$, cyclopropylboronic acid (1.1 mmol), heteroaryl triflate (1.0 mmol), 3.3 equiv. $KF \cdot 2H_2O$ and 1 equiv. NaBr in toluene (4 ml). [b] Isolated yield based on heteroaryl triflate. [c] ee: 89%, determined by HPLC (Chiralcel OJ), $[\alpha]_D^{20} = -302.4$ (*c*: 0.81 in $CHCl_3$). [d] ee: 93%, determined by HPLC (Chiralcel OJ) $[\alpha]_D^{20} = +311.5$ (*c*: 0.29 in $CHCl_3$). [e] ee: 89%, determined by HPLC (Chiralcel OD), $[\alpha]_D^{20} = -700.1$ (*c*: 0.58 in $CHCl_3$). [f] ee: 94%, determined by HPLC (Chiralcel OD), $[\alpha]_D^{20} = +710.4$ (*c*: 0.56 in $CHCl_3$).



3a

Scheme 1

propylboronic acids. The results are summarized in Table 2, where it can be seen that the yields were moderate to good.

The ^{1}H-NMR spectra and HPLC of all products showed clearly that they were pure *trans*-isomers. The configuration of the *trans*-cyclopropane was further determined by the ^{1}H-^{1}H NOESY spectrum of **3a** (Scheme 1), the most downfield cyclopropane proton H^d can be assigned easily for its NOE effect with the proton H^e on the pyridyl group. In addition there were strong NOE effects between H^b and H^d; H^b and H^c; H^a and H^c, but no NOE effects between H^d and H^a; H^d and H^c; H^a and H^b. These observations suggested that **3a** was pure 2-*trans*-cyclopropyl-substituted pyridine.

To further confirm this deduction an X-ray crystallographic study of compound **3g** was performed. A crystal of **3g** suitable for an X-ray analysis was obtained by crystallization in Et_2O. All measurements were made on a Rigaku AFC7R diffractometer with graphite monochromated Mo-Kα radiation and a 12 kW rotating anode generator. The crystal structure analysis of product **3g** gave: empirical formula $C_{18}H_{15}N$, formula weight 245.33, crystal system triclinic, space group $P\bar{1}$ (no. 2), $Z = 4$, $a = 12.064(3)$, $b = 12.797(2)$, $c = 9.794(3)$ Å, $\alpha = 102.99(2)$, $\beta = 97.17(2)$, $\gamma = 68.70(2)°$, $u = 1371.1(6)$ Å^3, $\mu = 0.69$ mm^{-1}, $T = 20 \pm 1$ °C, measured reflections 3470, independent reflections 3265 ($R_m = 0.040$), final $R = 0.041$, $R_w = 0.045$. The X-ray crystallographic structure (Fig. 1) of **3g** shows clearly that the configuration of the cyclopropane is *trans*, meaning that the configuration of the cyclopropyl group was retained during the reaction.

When using an optically active cyclopropylboronic acid[8c] as the reactant, the coupling products were also the pure *trans* isomers, judging from their ^{1}H-NMR spectra. Furthermore, the coupling products of aryl triflate/heteroaryl triflate with the same optically active cyclopropylboronic acid not only have the same ee value but also have the same optical activity[11] (Scheme 2). Therefore, the absolute configuration of the cyclopropyl group is confirmed to be retained during the coupling reaction, as in the results obtained in previous studies.[8c,12]

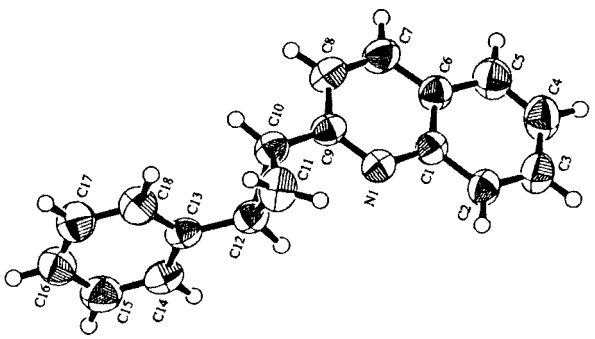
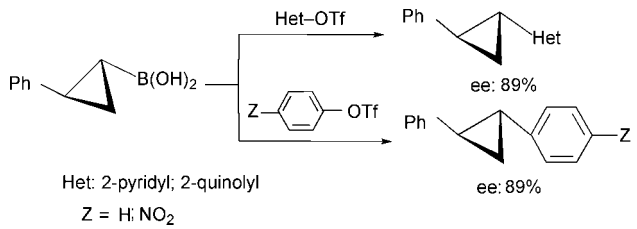


Fig. 1 Molecular structure of product **3g**.



Scheme 2

In conclusion, we have for the first time studied the cross-coupling reaction of heteroaryl triflates[13] with cyclopropylboronic acids. This reaction provides a novel and convenient method to prepare stereodefined cyclopropyl-substituted heteroarenes. The biological activities of these compounds are being studied.

Experimental

All reactions were performed under an argon atmosphere. The aryl triflates were prepared according to the literature procedure.[13] Melting points are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker AMX-300 (300 MHz), using $CDCl_3$ as the solvent with TMS as an internal standard. MS spectra were obtained with an HP5989A spectrometer using EI ionization at 70 eV. Elemental analyses were conducted using a Foss–Heracus Vario EL instrument. IR spectra were recorded on a Shimadzu IR-440 infrared spectrometer. Optical rotations were measured using a Perkin–Elmer 241 MM polarimeter with a thermally jacketed 10 cm cell at 20 °C. The ee values were determined by chiral HPLC on Chiralcel OD and Chiralcel OJ columns.

General procedure for the coupling reaction

Heteroaryl triflate (1 mmol), cyclopropylboronic acid (1.1 mmol), $Pd(PPh_3)_4$ (35 mg, 0.03 mmol), $KF \cdot 2\ H_2O$ (310 mg, 3.3 mmol) and NaBr (102 mg, 1 mmol) were placed in a flask under an argon atmosphere, then degassed toluene (4 ml) was added; the reaction mixture was stirred at 100 °C and monitored by TLC. After the reaction was complete, the reaction mixture was cooled to room temperature and 10 ml of water was added. The mixture was then extracted twice with petroleum (bp 60–90 °C) (2 × 15 ml). The combined organic layer was washed with brine (3 × 10 ml) and dried over $MgSO_4$. Removal of petroleum *in vacuo*, followed by silica gel chromatography [15–25% diethyl ether in petroleum (bp 60–90 °C)], gave the corresponding cyclopropyl-substituted heteroarenes **3a**–**i**.

3a. Liquid; IR ν_{max}/cm^{-1}: 2919; 1596; 1568; 1475; 1455; 772; 743. ^{1}H-NMR δ_H: 8.40 (d, 1H, $J = 4.5$); 7.48–7.54 (m, 1H); 7.08 (d, 1H, $J = 8.0$ Hz); 6.98–7.03 (m, 1H); 1.76 (ddd, 1H); 1.27–1.45 (m, 9H, 4 × CH_2 + H); 1.18–1.20 (m, 1H); 0.78–0.90 (m, 4H, CH_3 + H). ^{13}C-NMR δ: 163.0; 149.2; 135.7; 121.1; 120.0; 34.0; 31.7; 29.0; 25.0; 24.4; 22.7; 17.0; 14.1. MS(EI) *m*/*z*: 190 (100); 132 (92.45); 119 (62.12); 118 (54.74); 117 (39.85); 133 (27.30); 146 (17.23); 130 (16.18). Anal. calcd. for $C_{13}H_{19}N$: C%, 82.48, H%, 10.11, N%, 7.40. Found: C%, 82.26, H%, 10.27, N%, 7.58.

3b. Liquid; IR ν_{max}/cm^{-1}: 2921; 1597; 1569; 1478; 1457; 771; 742. ^{1}H-NMR δ_H: 8.40 (d, 1H, $J = 4.5$); 7.47–7.54 (m, 1H); 7.08 (d, 1H, $J = 8.0$ Hz); 6.99–7.04 (m, 1H); 1.76 (ddd, 1H); 1.26–1.43 (m, 7H, 3 × CH_2 + H); 1.18–1.20 (m, 1H); 0.78–0.89 (m, 4H, CH_3 + H). MS(EI) *m*/*z*: 132 (100); 118 (64.55); 119 (56.76); 117 (48.26); 93 (33.52); 105 (29.30); 133 (25.29); 79 (23.80). Anal. calcd. for $C_{12}H_{17}N$: C%, 82.22, H%, 9.78, N%, 7.99. Found: C%, 81.92, H%, 9.98, N%, 7.98.

3c. Liquid; IR ν_{max}/cm^{-1}: 3001; 1597; 1567; 1478; 1444; 743; 699. ^{1}H-NMR δ_H: 8.51 (d, 1H, $J = 4.5$ Hz); 7.53–7.58 (m, 1H); 7.05–7.43 (m, 7H); 2.57 (ddd, 1H); 2.31 (ddd, 1H); 1.80 (ddd, 1H); 1.49 (ddd, 1H). MS(EI) *m*/*z*: 194 (100); 195 (80.40); 93 (33.30); 196 (21.64); 193 (20.74); 118 (18.85); 180 (16.76); 167 (12.76). Anal. calcd. for $C_{14}H_{13}N$: C%, 86.12, H%, 6.71, N%, 7.17. Found: C%, 85.67, H%, 6.95, N%, 7.31.

3d. Liquid; IR ν_{max}/cm^{-1}: 2933; 1625; 1608; 1508; 1433; 827; 756. ^{1}H-NMR δ_H: 7.96–8.00 (m, 2H); 7.74 (d, 1H, $J = 8.1$); 7.62–7.67 (m, 1H); 7.40–7.45 (m, 1H); 7.12 (d, 1H,

$J = 8.5$ Hz); 1.99 (ddd, 1H); 1.26–1.53 (m, 8H, 3 × CH_2 + H + H); 0.82–0.95 (m, 4H, CH_3 + H). MS(EI) m/z: 168 (100); 182 (99.44); 169 (90.88); 167 (87.16); 183 (36.62); 180 (28.70); 143 (28.39). Anal. calcd. for $C_{16}H_{19}N$: C%, 85.29, H%, 8.50, N%, 6.22. Found: C%, 85.58, H%, 8.94, N%, 6.01.

3e. Liquid; IR ν_{max}/cm^{-1}: 2931; 1623; 1607; 1507; 1431; 826; 757. ^{1}H-NMR δ_H: 7.93–7.96 (m, 2H); 7.71 (d, 1H, $J = 8.1$); 7.59–7.65 (m, 1H); 7.37–7.42 (m, 1H); 7.11 (d, 1H, $J = 8.6$ Hz); 1.96 (ddd, 1H); 1.29–1.50 (m, 10H, 4 × CH_2 + H + H); 0.85–0.94 (m, 4H, CH_3 + H). MS(EI) m/z: 168 (100); 169 (97.20); 182 (96.58); 167 (78.68); 240 (38.41); 183 (29.35); 143 (28.54); 180 (24.77). Anal. calcd. for $C_{17}H_{21}N$: C%, 85.31, H%, 8.84, N%, 5.85. Found: C%, 85.14, H%, 8.83, N%, 5.90.

3f. Liquid; IR ν_{max}/cm^{-1}: 2927; 1621; 1605; 1505; 1434; 828; 758. ^{1}H-NMR δ_H: 7.93–7.96 (m, 2H); 7.71 (d, 1H); 7.59–7.65 (m, 1H); 7.37–7.42 (m, 1H); 7.11 (d, 1H); 1.97 (ddd, 1H); 1.25–1.50 (m, 12H, 5 × CH_2 + H + H); 0.85–0.94 (m, 4H, CH_3 + H). MS(EI) m/z: 182 (100); 168 (93.46); 169 (93.25); 167 (67.94); 143 (37.96); 155 (24.75); 196 (22.23); 156 (21.12). Anal. calcd. for $C_{18}H_{23}N$: C%, 85.32, H%, 9.15, N%, 5.53. Found: C%, 85.17, H%, 9.26, N%, 5.70.

3g. White solid, mp: 70–72 °C; IR ν_{max}/cm^{-1}: 3007; 1618; 1600; 1560; 1503; 1496; 1196; 819; 757. ^{1}H-NMR (400 MHz) δ_H: 7.96–8.00 (m, 2H); 7.64–7.73 (m, 2H); 7.42–7.44 (m, 1H); 7.17–7.30 (m, 6H); 2.65–2.69 (ddd, 1H,); 2.44–2.48 (ddd, 1H); 1.96–1.99 (ddd, 1H); 1.54–1.57 (ddd, 1H). MS(EI) m/z: 244 (100); 245 (65.49); 143 (21.66); 246 (12.04); 168 (9.99); 242 (9.71); 167 (7.86); 230 (7.18). Anal. calcd. for $C_{18}H_{15}N$: C%, 88.13, H%, 6.16, N%, 5.71. Found: C%, 87.90, H%, 6.13, N%, 5.74.

CCDC reference number 440/169. See http://www.rsc.org/suppdata/nj/b0/b001501k/ for crystallographic files in .cif format.

3h. Liquid; IR ν_{max}/cm^{-1}: 2914; 1599; 1500; 1467; 1368; 823; 795. ^{1}H-NMR δ_H: 8.98 (d, 1H, $J = 4.1$); 8.13 (d, 1H, $J = 8.3$); 7.60 (d, 1H, $J = 8.1$); 7.38–7.46 (m, 2H); 7.15 (d, 1H, $J = 7.2$); 3.00 (ddd, 1H); 1.25–1.55 (m, 7H, 3 × CH_2 + H); 0.96–1.04 (m, 2H, H + H); 0.90 (t, 3H, $J = 7.2$ Hz). MS(EI) m/z: 154 (100); 168 (91.77); 167 (66.93); 182 (46.39); 169 (44.10); 226 (29.76); 155 (27.59); 225 (15.32). Anal. calcd. for $C_{16}H_{19}N$: C%, 85.29, H%, 8.49, N%, 6.22. Found: C%, 85.23, H%, 8.54, N%, 6.39.

3i. Liquid; IR ν_{max}/cm^{-1}: 2917; 1600; 1501; 1472; 1372; 824; 797. ^{1}H-NMR δ_H: 8.97 (d, 1H, $J = 4.0$); 8.11 (d, 1H, $J = 8.2$); 7.58 (d, 1H, $J = 8.2$); 7.34–7.45 (m, 2H); 7.13 (d, 1H, $J = 7.2$); 3.01 (ddd, 1H); 1.25–1.55 (m, 11H, 5 × CH_2 + H); 0.96–1.04 (m, 2H, H + H); 0.87 (t, 3H, $J = 6.8$ Hz). MS(EI) m/z: 154 (100); 168 (95.86); 167 (89.15); 182 (53.80); 169 (43.94); 155 (33.69); 253 (18.12); 252 (17.19). Anal. calcd. for $C_{18}H_{23}N$: C%, 85.32, H%, 9.15, N%, 5.53. Found: C%, 85.41, H%, 8.96, N%, 5.30.

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Notes and references

1 (*a*) J. D. White, T.-S. Kim and M. Nambu, *J. Am. Chem. Soc.*, 1997, **119**, 103 and references cited therein; (*b*) A. D. Rodríguez, J.-G. Shi and S. D. Huang, *J. Org. Chem.*, 1998, **63**, 4425.

2 (*a*) D. W. Brooks, B. W. Horrom, K. E. Rodriques and Mazdiyasni (Abbott Laboratories), *Eur. Pat.* 436199, 1991; *Chem. Abstr.*, 1991, **115**, 279483; (*b*) M. Suzuki, K. Tanikawa and K. Sakoda, *Heterocycles*, 1999, **50**, 479.

3 (*a*) H. N. C. Wong, M.-Y. Hon, C.-W. Tse, Y. C. Yip, J. Tanko and T. Hudlicky, *Chem. Rev.*, 1989, **89**, 165; (*b*) J. R. Y. Salaun, *Top. Curr. Chem.*, 1988, **144**, 1.

4 (*a*) A. B. Charrette and P. Chua, *J. Org. Chem.*, 1998, **63**, 908; (*b*) J. Bivin, J. Pothier and S. Z. Zard, *Tetrahedron Lett.*, 1999, **40**, 3701; (*c*) F. Freeman, T. Chen and J. B. Linden, *Synthesis*, 1997, 861.

5 (*a*) D. W. Gordon, *Synlett*, 1996, 893; (*b*) C. N. Johnson, G. Stemp, N. Anand, S. C. Stephen and T. Gallagher, *Synlett*, 1998, 1025; (*c*) O. Lohse, P. Thevenin and E. Waldvogel, *Synlett*, 1999, 45; (*d*) I. Collins and J. L. Castro, *Tetrahedron Lett.*, 1999, **40**, 4069.

6 (*a*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457; (*b*) A. Suzuki, *J. Organomet. Chem.*, 1999, **576**, 147.

7 (*a*) X.-Z. Wang and M.-Z. Deng, *J. Chem. Soc., Perkin. Trans. 1*, 1996, 2663; (*b*) J. P. Hildebrand and S. P. Marsden, *Synlett*, 1996, 893; (*c*) A. B. Charrette and R. P. DeFreitas–Gil, *Tetrahedron Lett.*, 1997, **38**, 2809; (*d*) M.-L. Yao and M.-Z. Deng, *Synthesis*, 2000, in press.

8 (*a*) H. Imai and S. N. Mineta, *J. Org. Chem.*, 1990, **55**, 4986; (*b*) J. Pietruszka and M. Widenmeyer, *Synlett*, 1997, 977; (*c*) S.-M. Zhou, M.-Z. Deng, L.-J. Xia and M.-H. Tang, *Angew. Chem., Int. Ed.*,, 1998, **37**, 2845; (*d*) J. E. A. Luithle and J. Pietruszka, *J. Org. Chem.*, 1999, **64**, 8287.

9 H.-R. Ma, X.-H. Wang and M.-Z. Deng, *Synth. Commun.*, 1999, **29**, 2477.

10 V. Percec, J.-Y. Bae and D. H. Hill, *J. Org. Chem.*, 1995, **60**, 1060.

11 (1*R*,2*R*)-1,2-Diphenylcyclopropane: $[\alpha]_D^{20} = -356.2$ (*c* 0.78 in $CHCl_3$), ee: 89%; $\mathbf{3c}_{(1R,2R)}$: $[\alpha]_D^{20} = -302.4$ (*c* 0.81 in $CHCl_3$), ee: 89%; $\mathbf{3g}_{(1R,2R)}$: $[\alpha]_D^{20} = -700.1$ (*c* 0.58 in $CHCl_3$), ee: 89%.

12 (*a*) B. H. Ridgway and K. A. Woerpel, *J. Org. Chem.*, 1998, **63**, 458; (*b*) K. Matos and J. A. Soderquist, *J. Org. Chem.*, 1998, **63**, 461.

13 (*a*) P. J. Stang, M. Hanack and L. R. Subramanian, *Synthesis*, 1982, 85; (*b*) K. Ritter, *Synthesis*, 1993, 735.