Convenient Route to 2-(Trialkylstannyl)cyclopropylamines and Their Application in Palladium-Catalyzed Cross-Coupling Reactions[‡]

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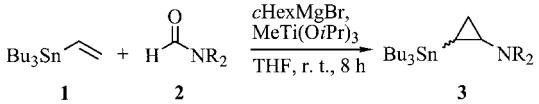
The 2-(trialkylstannyl)-*N*,*N*-dialkylcyclopropylamines **3** were obtained by titanium-mediated aminocyclopropanation of tributylvinylstannane with *N*,*N*-dialkylformamides in yields of 80–84% and with excellent diastereoselectivities (*trans*/*cis* > 45:1). The resulting stannanes could advantageously be applied in Stille cross-coupling reactions with aryl iodides, providing the pure *trans*-2-aryl-(*N*,*N*-dialkylamino)cyclopropanes **8** in yields ranging from 45 to 67% (six examples). The coupling of ethyl (*E*)-3-iodoacrylate (**9**) gave ethyl *cis*-5-(dibenzylamino)cyclopent-2-enecarboxylate (**10**) as a single diastereomer in 54% yield.

Introduction

Among the various cyclopropane derivatives, cyclopropylamines constitute one of the more important classes, both in view of their roles as key elements in biologically active compounds[1,2] and as theoretically interesting molecules.[3] The titanium-mediated reductive cyclopropanation of *N*,*N*-dialkylcarboxamides developed in recent years[4,5] has significantly improved the accessibility of various cyclopropylamines. Except in a few cases, however, this method has the drawback of yielding 2-substituted cyclopropylamines with only low or moderate degrees of diastereoselectivity. In contrast, the corresponding titanium-mediated transformation of esters into cyclopropanols yielded *trans*-2-substituted (referring to the positions of the hydroxy and the 2-substituent) derivatives completely diastereoselectively.[5] Complete diastereoselectivity in cyclopropylamine formation has only been observed in reductive aminocyclopropanation of trimethylsilylethylene with *N*,*N*-dialkylformamides.[6] Since the electronic effect of a trialkylsilyl group is in general more important than its steric bulk in determining the stereochemical outcome of a reaction,[7] one might expect that a trialkylstannyl group should be at least as effective in favoring the formation of a *trans* diastereomer. We therefore tested the preparation of 2-(trialkylstannyl)cyclopropylamines by aminocyclopropanation with *N*,*N*-dialkylformamides of trialkylvinylstannanes via ligand-exchanged titanacyclopropanes.[6,8]

Results and Discussion

In application of the previously developed procedure,[6] tributylvinylstannane was treated with cyclohexylmagnesium bromide in the presence of methyltriisopropyloxytitanium and an *N*,*N*-dialkylformamide **2**. After some optimization of conditions, the 2-(tributylstannyl)-*N*,*N*-dialkylcyclopropylamines **3a** and **3b** were obtained not only in good yields (80 and 84%, respectively), but also with excellent *trans* diastereoselectivities, with diastereomeric excesses > 95% (Scheme 1).



1 **2** **3**

3	R	(%)	*cis*/*trans*
a	Bn	92	1 : 45
b	Me	88	<1 : 50

Scheme 1. Synthesis of 2-(trialkylstannyl)-*N*,*N*-dialkylcyclopropylamines **3**

This would best be explained by assuming that the insertion of the dialkylformamide carbonyl group occurs prefer-

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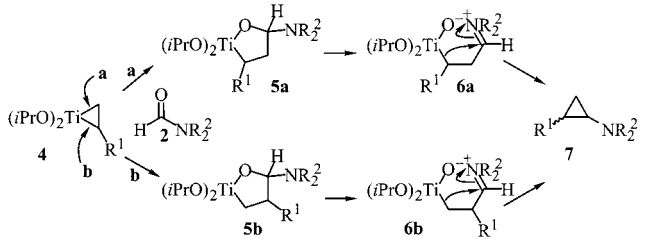
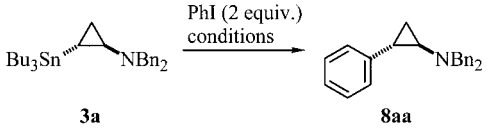
entially, for electronic reasons, into the more highly substituted titanium-carbon bond of the titanacyclopropane intermediate **4** (Scheme 2, mode **b**) when R^1 is a trialkylstannyl (or a trialkylsilyl) group, resulting in an oxatitanacyclopentane intermediate **5b**. This would open up to give an iminium-titanium oxide zwitterion **6b**, in which R^1 is adjacent to the iminium ion moiety. In this situation, the stereochemical information on the substituted carbon would translate more efficiently onto the stereogenic center newly formed upon ring closure to the 2-substituted cyclopropylamine **7** (Scheme 2). It is obvious that in the ring closure of the corresponding zwitterion **6a**, formed via **5a** after insertion of the formamide into the least substituted Ti−C bond in **4** (mode **a**), the 1,3-relationship of the old and the newly formed stereogenic center should result in weaker stereocontrol. However, in view of the fact that titanacyclopropenes from alkynyltributylstannanes undergo insertion of aldehydes only into the titanium-carbon bond not bearing the tin substituent[9] (corresponding to mode **a** in Scheme 2), this explanation becomes less probable. It is also known that silyl-substituted titanacyclopropane intermediates react with aldehydes only according to insertion mode **a**.[10] After all, the high diastereoselectivity observed in the conversion of *N*,*N*-dialkylformamides with vinylstannanes to 2-stannylcyclopropylamines may simply be due to the steric bulk of the trialkylstannyl group. A control experiment with 3,3-dimethylbut-1-ene (*tert*-butylethene) also gave only *trans*-*N*,*N*-dibenzyl-2-*tert*-butylcyclopropylamine, but in poor yield (19%) and an impure state.



Scheme 2

Cyclopropylstannanes, although not amino-substituted ones, have previously been used as versatile building blocks for the construction of other cyclopropane derivatives; examples include palladium-catalyzed oxidative homocoupling to yield bicyclopropyl derivatives[11] and destannylative transformation,[12] as well as transmetallations with subsequent electrophilic substitution[13] or cross-coupling reactions.[14] A few examples of direct palladium-catalyzed cross-coupling reactions of cyclopropylstannanes have also been reported.[15,16] To test this possibility with the readily available aminocyclopropylstannanes **3**, the dibenzylamino derivative **3a** was treated with phenyl iodide under typical conditions for the cross coupling of aryl and vinylstannanes. The initial results were disappointing, but the cross-coupling product **8aa** was eventually obtained in 48% yield through the use of a procedure previously developed by Farina et al.[17] (Scheme 3 and Table 1, conditions **A**).



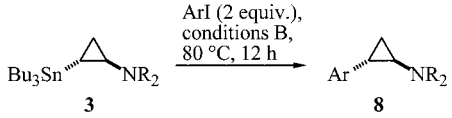
Scheme 3. Cross coupling of cyclopropylstannane **3a** with phenyl iodide; for details see Table 1

By modifying the conditions, especially by switching to palladium acetate as the catalyst precursor and optimizing the temperature, the yield could be raised to 67% (Entry 3 in Table 1). A temperature of 80 °C turned out to be the optimum, any further increase resulting in destannylation as a competing side reaction.

Table 1. Palladium-catalyzed cross coupling of cyclopropylstannane **3a** with phenyl iodide (see Scheme 3). **A**: $[Pd_2dba_3]\cdot CHCl_3$ (10 mol %), $AsPh_3$ (15 mol %), CuI (5 mol %), LiCl (3 equiv.), DMF, 12 h; **B**: as **A**, but with $Pd(OAc)_2$ (5 mol %); **C**: as **B**, but in *N*-methylpyrrolidinone (NMP)

Entry	Conditions	Temperature [°C]	Yield (%)
1	**A**	65	48
2	**A**	80	56
3	**B**	80	67
4	**B**	100	48
5	**B**	120	19
6	**C**	80	13

Various aryl iodides were coupled to **3a** and **3b** (Scheme 4) according to the optimized procedure. While *meta*- and *para*-substituted aryl iodides gave the corresponding 2-arylcyclopropylamines in moderate to good yields, *ortho*-iodotoluene failed to furnish any coupling product.

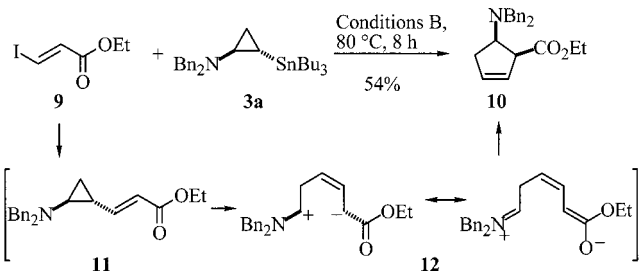


3	R	Ar	**8**	(%)
a	Bn	Ph	**aa**	67
a	Bn	2-MeC_6H_4	**ab**	–
a	Bn	4-MeC_6H_4	**ac**	65
b	Me	4-MeC_6H_4	**bc**	63
a	Bn	3,5*t*Bu-C_6H_3	**ad**	63
a	Bn	4-MeOOCC_6H_4	**ae**	45
a	Bn	4-MeOC_6H_4	**af**	49

Scheme 4. Palladium-catalyzed cross-couplings of 2-(trialkylstannyl)-*N*,*N*-dialkylcyclopropylamines **3** with various aryl iodides under optimized conditions B (see Table 1)

Surprisingly, ethyl *trans*-3-iodoacrylate (**9**) did not provide the expected 3-(aminocyclopropyl)acrylate **11**, but instead gave ethyl *cis*-5-(dibenzylamino)cyclopent-2-enecar-

boxylate (**10**) as a single diastereomer. The same product was obtained with ethyl *cis*-3-iodoacrylate, but in very low yield (5%). Most probably, the coupling product **11** is initially formed, but, being a donor-acceptor-substituted cyclopropane derivative,[18] undergoes rapid ring-opening to the zwitterionic intermediate **12** under the conditions employed. Because of the attractive interaction between the termini in this iminium enolate, the ring-closure places the two substituents on the same side of the ring.



Scheme 5. Cross coupling of *N*,*N*-dibenzyl-2-(tributylstannyl)cyclopropylamine (**3a**) with ethyl *trans*-3-iodoacrylate (**9**) and subsequent rearrangement to yield ethyl *cis*-5-(dibenzylamino)cyclopent-2-enecarboxylate (**10**)

This coupling-rearrangement sequence constitutes a diastereoselective synthesis of an interesting β-aminocyclopentenecarboxylic acid in a protected form. The facility of this stereoselective approach to a synthetically useful cyclopentene derivative warrants further investigations into coupling reactions of the readily available aminocyclopropylstannanes, with, for example, various functionally substituted iodoalkenes[14a] and β-iodo-substituted α,β-unsaturated carbonyl compounds.[14b]

Experimental Section

General Remarks: All chemicals were used as commercially available. All reactions were performed in anhydrous solvents under N_2. Ethereal solvents were dried under N_2 with sodium. Reactions were monitored by thin-layer chromatography on silica gel plates (Macherey−Nagel SIL G/UV$_{254}$). The chromatograms were viewed under UV light or by spraying with ninhydrin. Silica gel 60 (0.063−0.200 mm, 230−400 mesh) obtained from E. Merck, Darmstadt (VWR Intl) was used for column chromatography. Eluents were distilled before use. NMR spectra were recorded with a Bruker AM 250 instrument at 250 MHz (^{1}H) and at 62.9 MHz (^{13}C) in $CDCl_3$. Chemical shifts δ are reported in ppm with C*H*Cl$_3$ (^{1}H, 7.26 ppm) and *C*DCl$_3$ (^{13}C, 77.0 ppm) as internal standards. ^{13}C NMR spectral assignments are supported by DEPT analysis, "+" designates CH or CH$_3$, "−" designates CH$_2$, and C$_{quat.}$ stands for quaternary carbon atoms. Infrared spectra were recorded with a Bruker IFS 66 (FT-IR) instrument. Mass spectra were obtained with Varian MAT CH 7, MAT 731, and Varian MAT 311 A (for HRMS) instruments. High-resolution mass spectra (HRMS) were obtained by use of a preselected-ion peak matching at R = 10000 to be within ± 2 ppm of the exact mass.

***N*,*N*-Dibenzyl-2-(tributylstannyl)cyclopropylamine (3a):** Tributylvinylstannane (3.2 g, 10 mmol) and then methyltriisopropyloxytitanium (4.8 g, 20 mmol) were added to a solution of dibenzylformamide (4.5 g, 20 mmol) in THF (20 mL). A solution of cyclohexylmagnesium bromide (0.8 M in THF, 31 mL, 25 mmol) was then added carefully. The resulting dark mixture was stirred at ambient temperature for 8 h. The reaction was quenched by careful addition of H_2O (2 mL), and the mixture was filtered. The residue was washed with diethyl ether (3 × 10 mL), and the two layers were separated. The aqueous phase was extracted with diethyl ether (2 × 10 mL), and the combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography by elution with pentane/diethyl ether 100:1, affording two fractions.

Fraction I (R_f = 0.76): *cis*-*N*,*N*-dibenzyl-2-(tributylstannyl)cyclopropylamine (60 mg, 1%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3081 cm^{-1}, 3062, 3028, 2955, 2922, 2870, 2853, 1494, 1451, 747, 698. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.03 (ddd, ^3J = 7.0, ^2J = 8.1, ^3J = 10.4 Hz, 1 H, 3-H), 0.27 (ddd, ^3J = 3.7, ^3J = 4.0, ^2J = 8.1 Hz, 1 H, 3-H), 0.79 (ddd, ^3J = 4.0, ^3J = 6.6, ^3J = 10.4 Hz, 1 H, 2-H), 0.89 (t, ^3J = 7.0 Hz, 9 H, 4′-H), 0.91 (t, ^3J = 5.8 Hz, 6 H, 1′-H), 1.31 (tq, ^3J = 7.0, ^3J = 7.9 Hz, 6 H, 3′-H), 1.50 (tt, ^3J = 5.8, ^3J = 7.9 Hz, 6 H, 2′-H), 2.09 (ddd, ^3J = 3.7, ^3J = 6.6, ^3J = 7.0 Hz, 1 H, 1-H), 3.55 (AB, d, ^2J = 13.7 Hz, 2 H, NCH$_2$), 3.75 (AB, d, ^2J = 13.7 Hz, 2 H, NCH$_2$), 7.22−7.39 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 9.9 (+, 3 C, C-4′), 11.8 (−, 1 C, C-3), 13.7 (−, 3 C, C-1′), 14.1 (+, 1 C, C-2), 27.5 (−, 3 C, C-3′), 29.2 (−, 3 C, C-2′), 40.2 (+, 1 C, C-1), 57.0 (−, 2 C, NCH$_2$), 126.7 (+, 2 C, Ph−C), 127.9 (+, 4 C, Ph−C), 129.6 (+, 4 C, Ph−C), 137.9 (C$_{quat.}$, 2 C, Ph−C) ppm. MS (CI, 70 eV): *m*/*z* (%) = 528 (100) [M$^+$ + 1], 438 (14), 308 (10), 238 (25), 198 (14), 163 (5), 146 (48), 106 (15).

Fraction II (R_f = 0.32): compound **3a** (4.89 g, 8.0 mmol, 92%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3085 cm^{-1}, 3062, 3027, 2957, 2925, 2871, 2852, 1494, 1454, 1029, 747, 698. ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.03 (ddd, ^3J = 4.9, ^2J = 7.6, ^3J = 10.4 Hz, 1 H, 3-H), 0.40 (ddd, ^3J = 4.0, ^3J = 5.8, ^2J = 7.6 Hz, 1 H, 3-H), 0.63 (ddd, ^3J = 3.4, ^3J = 4.0, ^3J = 10.4 Hz, 1 H, 2-H), 0.76 (t, ^3J = 7.9 Hz, 6 H, 1′-H), 0.89 (t, ^3J = 7.0 Hz, 9 H, 4′-H), 1.30 (tt, ^3J = 6.7, ^3J = 7.9 Hz, 6 H, 2′-H), 1.44 (tq, ^3J = 6.7, ^3J = 7.0 Hz, 6 H, 3′-H), 1.87 (ddd, ^3J = 3.4, ^3J = 4.9, ^3J = 5.8 Hz, 1 H, 1-H), 3.67 (AB, d, ^2J = 13.7 Hz, 2 H, NCH$_2$), 3.72 (AB, d, ^2J = 13.7 Hz, 2 H, NCH$_2$), 7.22−7.34 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 3.6 (+, 1 C, C-2), 8.7 (−, 3 C, C-1′), 12.2 (−, 1 C, C-3), 13.7 (+, 3 C, C-4′), 27.4 (−, 3 C, C-2′), 29.3 (−, 3 C, C-3′), 41.1 (+, 1 C, C-1), 58.7 (−, 2 C, NCH$_2$), 126.7 (+, 2 C, Ph−C), 127.9 (+, 4 C, Ph−C), 129.3 (+, 4 C, Ph−C), 139.1 (C$_{quat.}$, 2 C, Ph−C) ppm. MS (CI, 70 eV): *m*/*z* (%) = 528 (100) [M$^+$ + 1], 438 (5), 308 (10), 236 (55), 198 (3), 146 (15). $C_{29}H_{45}NSn$ (526.4): calcd. C 66.17, H 8.62, N 2.66; found C 65.87, H 8.32, N 2.58.

***trans*-*N*,*N*-Dimethyl-2-(tributylstannyl)cyclopropylamine (3b):** Tributylvinylstannane (3.2 g, 10 mmol) and then methyltriisopropyloxytitanium (4.8 g, 20 mmol) were added to a solution of dimethylformamide (1.5 g, 21 mmol) in THF (20 mL). A solution of cyclohexylmagnesium bromide (0.8 M in THF, 31 mL, 25 mmol) was then added carefully. The resulting dark mixture was stirred at ambient temperature for 8 h. The reaction was quenched by careful addition of H_2O (2 mL), and the mixture was filtered. The residue was washed with diethyl ether (3 × 10 mL), and the two layers were separated. The aqueous phase was extracted with diethyl ether (2 × 10 mL), and the combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography, eluting with pen-

tane/diethyl ether 10:1 (R_f = 0.14), to afford **3b** (3.34 g, 88%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3057 cm^{-1}, 2925, 2812, 2766, 1457, 1363, 1206, 1163, 921, 887, 754. ^1H NMR (250 MHz, $CDCl_3$): δ = −0.08 (ddd, ^3J = 5.2, ^2J = 7.6, ^3J = 11.3 Hz, 1 H, 3-H), 0.45 (ddd, ^3J = 4.0, ^3J = 6.1, ^2J = 7.6 Hz, 1 H, 3-H), 0.68 (ddd, ^3J = 3.7, ^3J = 4.0, ^3J = 11.3 Hz, 1 H, 2-H), 0.79 (t, ^3J = 7.6 Hz, 6 H, 1′-H), 0.88 (t, ^3J = 7.0 Hz, 9 H, 4′-H), 1.30 (tt, ^3J = 7.6, ^3J = 7.6 Hz, 6 H, 2′-H), 1.49 (tq, ^3J = 7.0, ^3J = 7.6 Hz, 6 H, 3′-H), 1.55 (ddd, ^3J = 3.7, ^3J = 5.2, ^3J = 6.1 Hz, 1 H, 1-H), 2.34 [s, 6 H, $N(CH_3)_2$]. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 2.5 (+, 1 C, C-2), 8.6 (+, 3 C, C-1′), 11.5 (−, 1 C, C-3), 13.7 (−, 3 C, C-4′), 27.4 (−, 3 C, C-2′), 29.1 (−, 3 C, C-3′), 44.3 (+, 1 C, C-1), 45.4 (+, 2 C, NCH_3). MS (CI, 70 eV): *m/z* (%) = 376/374 (100/77) [M^+], 308 (8), 200 (3), 100 (3), 84 (16). $C_{17}H_{37}NSn$ (374.2): calcd. C 54.57, H, 9.97, N 3.74; found C 54.32, H 9.69, N 3.70.

General Procedure for the Stille Coupling of 2-(Trialkylstannyl)cyclopropylamines 3 (GP): A solution of $Pd(OAc)_2$ (11 mg, 0.05 mmol, 5 mol %), CuI (10 mg, 53 μmol, 5 mol %), triphenylarsane (45 mg, 0.15 mmol, 15 mol %), lithium chloride (128 mg, 3 mmol), the cyclopropylstannane (1 mmol), and the aryl iodide (2 mmol) in DMF (10 mL) was placed in a Pyrex bottle and deoxygenated by passage of a stream of nitrogen through the solution for 30 min. The bottle was then carefully sealed and heated at 80 °C for 12 h. The mixture was poured into an aqueous ammonia solution (10%, 20 mL) and extracted with diethyl ether (3 × 50 mL). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography.

***trans*-*N*,*N*-Dibenzyl-2-phenylcyclopropylamine (8aa):** Treatment of **3a** (526 mg, 1 mmol) and iodobenzene (408 mg, 2 mmol) according to the GP gave **8aa** (210 mg, 67%) as a colorless solid after column chromatography (dichloromethane, R_f = 0.50), m.p. 49 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.97 (ddd, ^2J = 4.3, ^3J = 6.0, ^3J = 7.5 Hz, 1 H, 3-H), 1.05 (ddd, ^2J = 4.3, ^3J = 4.5, ^3J = 9.2 Hz, 1 H, 3-H), 1.82 (ddd, ^3J = 3.2, ^3J = 6.0, ^3J = 9.2 Hz, 1 H, 1-H), 2.04 (ddd, ^3J = 3.2, ^3J = 4.5, ^3J = 7.5 Hz, 1 H, 2-H), 3.67 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 3.79 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 6.70−6.87 (m, 2 H, Ph-H), 7.24−7.47 (m, 13 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 17.6 (−, 1 C, C-3), 26.4 (+, 1 C, C-2), 47.6 (+, 1 C, C-1), 58.4 (−, 2 C, NCH_2), 125.3 (+, 2 C, Ph−C), 125.7 (+, 1 C, Ph−C), 126.9 (+, 4 C, Ph−C), 128.0 (+, 2 C, Ph−C), 128.1 (+, 4 C, Ph−C), 129.4 (+, 2 C, Ph−C), 138.7 ($C_{quat.}$, 2 C, Ph−C), 142.1 ($C_{quat.}$, 1 C, Ph−C) ppm. $C_{23}H_{23}N$ (313.4): calcd. C 88.14, H 7.40, N 4.47; found C 87.94, H 7.17, N 4.32.

***trans*-*N*,*N*-Dimethyl-2-phenylcyclopropylamine (8ba):** Treatment of **3b** (375 mg, 1 mmol) and iodobenzene (408 mg, 2 mmol) according to the GP gave **8ba** (95 mg, 59%) as a colorless oil after column chromatography (diethyl ether, R_f = 0.30). IR (film): $\tilde{\nu}$ = 3060 cm^{-1}, 2939, 2815, 2771, 1499, 1453, 1213, 783, 742, 697. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.96 (ddd, ^2J = 4.4, ^3J = 5.8, ^3J = 6.9 Hz, 1 H, 3-H), 1.11 (ddd, ^3J = 4.3, ^2J = 4.4, ^3J = 9.3 Hz, 1 H, 3-H), 1.81 (ddd, ^3J = 3.2, ^3J = 4.3, ^3J = 6.9 Hz, 1 H, 2-H), 1.98 (ddd, ^3J = 3.2, ^3J = 5.8, ^3J = 9.3 Hz, 1 H, 1-H), 2.40 (s, 6 H, NCH_3), 7.04−7.30 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 17.2 (−, 1 C, C-3), 25.2 (+, 1 C, C-2), 45.0 (+, 2 C, NCH_3), 50.2 (+, 1 C, C-1), 125.6 (+, 1 C, Ph−C), 126.0 (+, 2 C, Ph−C), 128.2 (+, 2 C, Ph−C), 142.1 ($C_{quat.}$, 1 C, Ph−C) ppm. MS (EI, 70 eV): *m/z* (%) = 161 (100), 146 (20), 117 (21), 84 (39), 70 (97). $C_{11}H_{15}N$ (161.2): calcd. C 81.94, H 9.38, N 8.69; found C 81.62, H 9.58, N 8.55.

***trans*-*N*,*N*-Dibenzyl-2-(4′-methylphenyl)cyclopropylamine (8ac):** Treatment of **3a** (526 mg, 1 mmol) and 4-iodotoluene (436 mg, 2 mmol) according to the GP gave **8ac** (210 mg, 65%) as a colorless solid after column chromatography (dichloromethane, R_f = 0.64), m.p. 47 °C. IR (film): $\tilde{\nu}$ = 3061 cm^{-1}, 3027, 2922, 2801, 1517, 1453, 1120, 749, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.94 (ddd, ^2J = 4.3, ^3J = 5.8, ^3J = 7.5 Hz, 1 H, 3-H), 1.02 (ddd, ^2J = 4.3, ^3J = 4.5, ^3J = 9.1 Hz, 1 H, 3-H), 1.81 (ddd, ^3J = 3.1, ^3J = 5.8, ^3J = 9.1 Hz, 1 H, 1-H), 2.02 (ddd, ^3J = 3.1, ^3J = 4.5, ^3J = 7.5 Hz, 1 H, 2-H), 2.31 (s, 3 H, Ph−CH_3), 3.67 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 3.77 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 6.70−6.73 (m, 2 H, Ph-H), 7.00−7.04 (m, 2 H, Ph-H), 7.26−7.32 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 17.4 (−, 1 C, C-3), 21.0 (+, 1 C, Ph−CH_3), 26.0 (+, 1 C, C-2), 47.4 (+, 1 C, C-1), 58.4 (−, 2 C, NCH_2), 125.7 (+, 2 C, Ph−C), 126.8 (+, 2 C, Ph−C), 128.1 (+, 2 C, Ph−C), 128.7 (+, 4 C, Ph−C), 129.4 (+, 4 C, Ph−C), 134.8 ($C_{quat.}$, 1 C, Ph−C), 138.7 ($C_{quat.}$, 2 C, Ph−C), 139.0 ($C_{quat.}$, 1 C, Ph−C) ppm. MS (EI, 70 eV): *m/z* (%) = 327 (14) [M^+], 276 (5), 236 (65), 222 (22), 131 (15), 105 (53), 91 (100), 65 (6). $C_{24}H_{25}N$: 327.1987 (correct HRMS). $C_{24}H_{25}N$ (327.4): calcd. C 88.03, H 7.69, N 4.28; found C 88.11, H 7.43, N 4.21.

***trans*-*N*,*N*-Dimethyl-2-(4′-methylphenyl)cyclopropylamine (8bc):** Treatment of **3b** (375 mg, 1 mmol) and 4-iodotoluene (436 mg, 2 mmol) according to the GP gave **8bc** (110 mg, 63%) as a colorless oil after column chromatography (diethyl ether, R_f = 0.38). IR (film): $\tilde{\nu}$ = 3061 cm^{-1}, 1517, 1453, 1120, 749, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.93 (ddd, ^2J = 4.5, ^3J = 5.8, ^3J = 7.2 Hz, 1 H, 3-H), 1.08 (ddd, ^3J = 4.3, ^2J = 4.5, ^3J = 9.4 Hz, 1 H, 3-H), 1.77 (ddd, ^3J = 3.2, ^3J = 4.3, ^3J = 7.2 Hz, 1 H, 2-H), 2.02 (ddd, ^3J = 3.2, ^3J = 5.8, ^3J = 9.4 Hz, 1 H, 1-H), 2.31 (s, 3 H, Ph−CH_3), 2.39 (s, 6 H, NCH_3), 6.95−6.99 (m, 2 H, Ph-H), 7.05−7.11 (m, 2 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 17.0 (−, 1 C, C-3), 20.9 (+, 1 C, Ph−CH_3), 24.8 (+, 1 C, C-2), 45.0 (+, 2 C, NCH_3), 50.0 (+, 1 C, C-1), 126.0 (+, 2 C, Ph−C), 128.9 (+, 2 C, Ph−C), 135.1 ($C_{quat.}$, 1 C, Ph−C), 139.0 ($C_{quat.}$, 1 C, Ph−C) ppm. MS (EI, 70 eV): *m/z* (%) = 175 (57) [M^+], 160 (20), 131 (20), 105 (25), 84 (36), 70 (100). $C_{12}H_{17}N$ (175.3): calcd. C 82.23, H 9.78, N 7.99; found C 82.02, H 9.68, N 8.06.

***trans*-*N*,*N*-Dibenzyl-2-(3′,5′-di-*tert*-butylphenyl)cyclopropylamine (8ad):** Treatment of **3a** (526 mg, 1 mmol) and 3,5-di-*tert*-butyliodobenzene (632 mg, 2 mmol) according to the GP gave **8ad** (270 mg, 63%) as a colorless solid after column chromatography (diethyl ether/pentane, 1:10, R_f = 0.74), m.p. 72 °C. IR (KBr): $\tilde{\nu}$ = 3063 cm^{-1}, 3028, 2964, 2866, 1599, 1453, 1362, 1248, 1121, 748, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.97 (ddd, ^2J = 4.3, ^3J = 5.8, ^3J = 7.3 Hz, 1 H, 3-H), 1.04 (ddd, ^2J = 4.3, ^3J = 4.3, ^3J = 9.1 Hz, 1 H, 3-H), 1.34 [s, 18 H, $C(CH_3)_3$], 1.91 (ddd, ^3J = 3.6, ^3J = 5.8, ^3J = 9.1 Hz, 1 H, 1-H), 2.14 (ddd, ^3J = 3.6, ^3J = 4.3, ^3J = 7.3 Hz, 1 H, 2-H), 3.67 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 3.77 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 6.74 (d, ^4J = 1.8 Hz, 2 H, Ph-H), 7.24−7.36 (m, 11 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 17.7 (−, 1 C, C-3), 26.6 (+, 1 C, C-2), 31.5 [+, 6 C, $C(CH_3)_3$], 34.8 [$C_{quat.}$, 2 C, $C(CH_3)_3$], 47.4 (+, 1 C, C-1), 58.5 (−, 2 C, NCH_2), 119.7 (+, 1 C, Ph−C), 120.1 (+, 2 C, Ph−C), 126.8 (+, 2 C, Ph−C), 128.1 (+, 4 C, Ph−C), 129.4 (+, 4 C, Ph−C), 139.0 ($C_{quat.}$, 2 C, Ph−C), 141.0 ($C_{quat.}$, 2 C, Ph−C), 150.4 ($C_{quat.}$, 1 C, Ph−C) ppm. MS (EI, 70 eV): *m/z* (%) = 425 (22) [M^+], 391 (4), 334 (40), 222 (25), 210 (43), 146 (21), 91 (100), 57 (14). $C_{31}H_{39}N$: 425.3082 (correct HRMS). $C_{31}H_{39}N$ (425.7): calcd. C 87.47, H 9.24, N 3.29; found C 87.53, H 8.92, N 3.20.

***trans*-*N*,*N*-Dibenzyl-2-(4′-methoxycarbonylphenyl)cyclopropylamine (8ae):** Treatment of **3a** (526 mg, 1 mmol) and methyl 4-iodobenzoate (524 mg, 2 mmol) according to the GP gave **8ae** (167 mg, 45%) as a colorless solid after column chromatography (pentane/diethyl ether, 10:1, R_f = 0.34), m.p. 85 °C. IR (KBr): $\tilde{\nu}$ = 3023 cm^{-1}, 2949, 2918, 1723, 1609, 1440, 1281, 1183, 1117, 751, 707. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.90 (ddd, ^2J = 5.0, ^3J = 5.8, ^3J = 6.9 Hz, 1 H, 3-H), 1.12 (ddd, ^3J = 4.4, ^2J = 5.0, ^3J = 9.4 Hz, 1 H, 3-H), 1.75 (ddd, ^3J = 3.1, ^3J = 5.8, ^3J = 9.4 Hz, 1 H, 1-H), 2.10 (ddd, ^3J = 3.1, ^3J = 4.4, ^3J = 6.9 Hz, 1 H, 2-H), 3.54 (AB, d, ^2J = 9.2 Hz, 2 H, NCH_2), 3.65 (AB, d, ^2J = 9.2 Hz, 2 H, NCH_2), 3.91 (s, 3 H, OCH_3), 6.72−6.80 (m, 2 H, Ph-H), 7.21−7.39 (m, 10 H, Ph-H), 7.94−7.98 (m, 2 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 16.3 (−, 1 C, C-3), 25.8 (+, 1 C, C-2), 47.1 (+, 1 C, C-1), 51.8 (+, 1 C, OCH_3), 58.4 (−, 2 C, NCH_2), 113.5 (+, 2 C, Ph−C), 126.8 (+, 2 C, Ph−C), 126.9 (+, 2 C, Ph−C), 128.1 (+, 4 C, Ph−C), 129.4 (+, 4 C, Ph−C), 134.1 ($C_{quat.}$, 2 C, Ph−C), 138.7 ($C_{quat.}$, 1 C, Ph−C), 138.7 ($C_{quat.}$, 1 C, Ph−C), 166.3 ($C_{quat.}$, 1 C, COO) ppm. MS (EI, 70 eV): *m*/*z* (%) = 371 (9) [M^+], 280 (90), 222 (15), 175 (10), 149 (20), 106 (10), 91 (100), 65 (6). $C_{25}H_{25}NO_2$ (371.5): calcd. C 80.83, H 6.78, N 3.77; found C 81.10, H 6.70, N 3.59.

***trans*-*N*,*N*-Dibenzyl-2-(4′-methoxyphenyl)cyclopropylamine (8af):** Treatment of **3a** (526 mg, 1 mmol) and 4-iodoanisole (468 mg, 2 mmol) according to the GP gave **8af** (167 mg, 49%) as a colorless oil after column chromatography (dichloromethane, R_f = 0.72). IR (film): $\tilde{\nu}$ = 3062 cm^{-1}, 3028, 3002, 2923, 1833, 1611, 1515, 1247, 1177, 1038, 826, 749, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.94 (ddd, ^2J = 5.1, ^3J = 5.9, ^3J = 6.7 Hz, 1 H, 3-H), 1.02 (ddd, ^3J = 4.4, ^2J = 5.1, ^3J = 9.4 Hz, 1 H, 3-H), 1.81 (ddd, ^3J = 3.2, ^3J = 5.9, ^3J = 9.4 Hz, 1 H, 1-H), 2.02 (ddd, ^3J = 3.2, ^3J = 4.4, ^3J = 6.7 Hz, 1 H, 2-H), 3.67 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 3.79 (s, 3 H, OCH_3), 3.79 (AB, d, ^2J = 13.5 Hz, 2 H, NCH_2), 6.74−6.78 (m, 4 H, Ph-H), 7.23−7.36 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 17.0 (−, 1 C, C-3), 25.7 (+, 1 C, C-2), 47.3 (+, 1 C, C-1), 55.3 (+, 1 C, OCH_3), 58.4 (−, 2 C, NCH_2), 113.5 (+, 2 C, Ph−C), 126.8 (+, 2 C, Ph−C), 126.9 (+, 2 C, Ph−C), 128.1 (+, 4 C, Ph−C), 129.4 (+, 4 C, Ph−C), 134.1 ($C_{quat.}$, 2 C, Ph−C), 138.7 ($C_{quat.}$, 1 C, Ph−C), 138.7 ($C_{quat.}$, 1 C, Ph−C) ppm. MS (EI, 70 eV): *m*/*z* (%) = 343 (6) [M^+], 252 (27), 222 (13), 186 (10), 121 (68), 91 (100), 65 (15), 43 (7). $C_{24}H_{25}NO$: 343.1936 (correct HRMS).

Ethyl *cis*-5-(Dibenzylamino)-2-cyclopentenecarboxylate (10): Treatment of **3a** (526 mg, 1 mmol) and ethyl *trans*-3-iodoacrylate (452 mg, 2 mmol) according to the GP gave **10** (180 mg, 54%) as a colorless oil after column chromatography (diethyl ether/pentane, 1:10, R_f = 0.41). IR (film): $\tilde{\nu}$ = 3062 cm^{-1}, 2926, 1734, 1457, 1363, 1206, 1163, 1029, 742, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.1 Hz, 3 H, CH_3), 2.42 (ddddd, ^4J = 2.0, ^4J = 2.2, ^3J = 2.2, ^3J = 4.5, ^2J = 17.8 Hz, 1 H, 4-H), 2.67 (ddddd, ^4J = 2.4, ^4J = 2.4, ^3J = 2.5, ^3J = 8.7, ^2J = 17.8 Hz, 1 H, 4-H), 3.55 (AB, d, ^2J = 14.0 Hz, 2 H, NCH_2), 3.60 (AB, d, ^2J = 14.0 Hz, 2 H, NCH_2), 3.70 (ddddd, ^4J = 2.1, ^3J = 2.1, ^4J = 2.2, ^4J = 2.4, ^4J = 4.1 Hz, 1 H, 1-H), 3.93 (ddd, ^3J = 4.1, ^3J = 4.5, ^3J = 8.7 Hz, 1 H, 5-H), 4.11 (q, ^3J = 7.1 Hz, 2 H, OCH_2), 5.69 (dddd, ^4J = 2.1, ^3J = 2.2, ^3J = 2.5, ^3J = 6.0 Hz, 1 H, 3-H), 5.90 (dddd, ^4J = 2.0, ^3J = 2.1, ^4J = 2.4, ^3J = 6.0 Hz, 1 H, 2-H), 7.22−7.41 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, additional DEPT): δ = 14.2 (+, 1 C, CH_3), 35.5 (−, 1 C, C-4), 51.8 (+, 1 C, C-1), 53.9 (−, 2 C, NCH_2), 60.7 (−, 1 C, OCH_2), 62.2 (+, 1 C, C-5), 126.8 (+, 2 C, Ph−C), 127.9 (+, 1 C, C-3), 128.2 (+, 4 C, Ph−C), 128.6 (+, 4 C, Ph−C), 133.1 (+, 1 C, C-2), 139.7 ($C_{quat.}$, 2 C, Ph−C), 174.7 ($C_{quat.}$, 1 C, CO) ppm. MS (EI, 70 eV): *m*/*z* (%) = 335 (60) [M^+], 306 (46), 262 (36), 244 (31), 222 (4), 170 (6), 91 (100), 65 (6). $C_{22}H_{25}NO_2$: 335.1885 (correct HRMS).

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[1] [1a] J. Salaün, M. S. Baird, *Curr. Med. Chem.* **1995**, *2*, 511−542. [1b] J. Salaün, *Top. Curr. Chem.* **2000**, *207*, 1−67.
[2] Cf. foonote (1) in: M. L. Gillaspy, B. A. Lefker, W. A. Hada, D. J. Hoover, *Tetrahedron Lett.* **1995**, *36*, 7399−7402.
[3] A. de Meijere, V. Chaplinski, F. Gerson, P. Merstetter, E. Haselbach, *J. Org. Chem.* **1999**, *64*, 6951−6959.
[4] A. de Meijere, S. I. Kozhushkov, A. I. Savchenko, in *Titanium and Zirconium in Organic Synthesis* (Ed.: I. Marek), Wiley-VCH, Weinheim, **2002**, pp. 390−434.
[5] Review: O. G. Kulinkovich, A. de Meijere, *Chem. Rev.* **2000**, *100*, 2789−2834.
[6] A. de Meijere, C. M. Williams, A. Kourdioukov, S. V. Sviridov, V. Chaplinski, M. Kordes, A. I. Savchenko, C. Stratmann, M. Noltemeyer, *Chem. Eur. J.* **2002**, *8*, 3789−3801.
[7] I. Fleming, A. Barbero, D. Walter, *Chem. Rev.* **1997**, *97*, 2063−2192.
[8] For the use of vinylstannanes in the synthesis of vinylcyclopropanols see: K. Lee, S. Kim, J. K. Cha, *J. Org. Chem.* **1998**, *63*, 9135−9138.
[9] V. Launay, I. Beaudet, J.-P. Quintard, *Synlett* **1997**, 821−823.
[10] R. Mizojiri, H. Urabe, F. Sato, *J. Org. Chem.* **2000**, *65*, 6217−6222.
[11] T. Itoh, S. Emoto, M. Kondo, *Tetrahedron* **1998**, *54*, 5225−5232.
[12] M. Pohmakotr, A. Takampon, *Tetrahedron Lett.* **1996**, *37*, 4585−4588.
[13] M. Lautens, P. H. M. Delanghe, J. B. Goh, C. H. Zhang, *J. Org. Chem.* **1995**, *60*, 4213−4227.
[14] [14a] E. Piers, M. Jean, P. S. Marrs, *Tetrahedron Lett.* **1987**, *28*, 5075−5078. [14b] E. Piers, J. Banville, C. K. Lau, I. Nagakura, *Canad. J. Chem.* **1982**, *60*, 2965−2975.
[15] D. Peters, A. B. Hörnfeldt, S. Gronowitz, *J. Heterocycl. Chem.* **1991**, *28*, 1629−1631.
[16] W. D. Schmitz, D. Romo, *Tetrahedron Lett.* **1996**, *37*, 4857−4860.
[17] V. Farina, S. Kapadia, B. Krishnan, C. Wang, L. S. Liebeskind, *J. Org. Chem.* **1994**, *59*, 5905−5911.
[18] Reviews see: [18a] H.-U. Reißig, *Topics Curr. Chem.* **1988**, *144*, 73−135. [18b] H.-U. Reißig, R. Zimmer, *Chem. Rev.* **2003**, *103*, 1151−1196.

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