Supplementary Material (ESI) for Chemical Communications

SUPPORTING INFORMATION

One-Pot Approach for the Synthesis of *trans*-Cyclopropyl Compounds from Aldehydes. Application to the Synthesis of GPR40 Receptor Agonists

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GENERAL INFORMATION

Unless otherwise noted, all non-aqueous reactions were run under an inert atmosphere (argon) with rigid exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds.[1] All glassware was stored in the oven and/or was flame dried prior to use under an inert atmosphere of gas. The solvents were dried using standard methods prior to use. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel (Merck 60 F254). Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium molybdate, ethanolic phosphomolybdic acid, iodine, or aqueous potassium permanganate. Flash column chromatography was performed using 230-400 mesh silica (EM Science or Silicycle) of the indicated solvent system according to standard technique.[2] Melting points were obtained on a Buchi melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin Elmer Spectrum One FTIR and are reported in reciprocal centimeters (cm^{-1}). Only the most important and relevant frequencies are reported. Nuclear magnetic resonance spectra (^{1}H, ^{13}C, DEPT 135, COSY, HMQC, NOESY) were recorded either on a Bruker AV 300, AMX 300, AV 400 or ARX 400 spectrometer (300, 300, 400 et 400 MHz respectively) in deuterochloroform, unless otherwise noted. Chemical shifts for ^{1}H NMR spectra are recorded in parts per million (ppm) on the δ scale relative to an internal standard of residual solvent (chloroform, δ7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, integration, and assignment. Chemical shifts for 13C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (77.00 ppm) as the internal standard. All spectra were obtained with complete proton decoupling. When ambiguous, proton and carbon assignments were established using COSY, HMQC and DEPT experiments. High resolution mass spectra were performed by the Centre régional de spectroscopie de masse de l'Université de Montréal. Combustion analyses were performed by the Laboratoire d'analyse élémentaire de l'Université de Montréal. Copper(I) iodide CuI was purchased from Strem. The commercially available aldehydes were purified using standard methods prior to use. Triphenylphosphine was received from Aldrich Chemical Co and used without further purification.

CAUTION!!! Diazo compounds are toxic and potentially explosive. They should be stored in refrigerator and handled with caution in a fume hood. Ethyl diazoacetate is commercially available from Aldrich, but was prepared from ethyl glycinate hydrochloride according to the literature.[3] Diazomethane was prepared as a solution in dichloromethane (C = 0.30 to 0.50M).[4] Other diazo compounds methyl diazoacetate and *tert*-butyldiazoacetate,[5] diazoacetophenone,[6] *N*,*N*-dimethyl diazoacetamide and *N*-methoxy-*N*-methyl diazoacetamide,[7] dimethyl (diazomethyl)phosphonate[8] were prepared following literature procedure.

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1 Shriver, D. F.; Drezdzon, M. A. *The manipulation of air-sensitive compounds*; 2nd Edition ed.; Wiley: New York, 1986.

2 Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

3 Searle N. E. *Org. Synth.* Coll. Vol. IV, **1963**, 424.

4 de Boer T. J.; Backer, H. J. *Org. Synth.* Coll. Vol. IV, **1963**, 250.

5 Regitz, M.; Hocker, J.; Liedhegener A. *Org. Synth.* Coll. Vol. V, **1973**, 179.

6 Bridson, J.N.; Hooz J. *Org. Synth.* Coll. Vol. VI, **1988**, 386.

7 Bartlett, P.A.; Carruthers, N.I.; Winter, B. M.; Long, K.P. *J. Org. Chem.* **1982**, *47*, 1284-91.

8 Ohira, S. *Synth. Commun.* **1989**, *19*, 561-564.

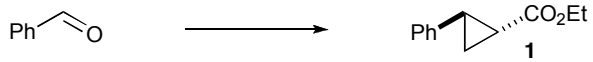
GENERAL PROCEDURES

Method A: Catalytic one-pot process in dichloromethane.
CuI (10 mg, 0.050 mmol) and triphenylphosphine (262 mg, 1.00 mmol) were placed in a vessel which was backfilled with argon. Dichloromethane (4.0 mL) was added and the resulting solution was stirred for 5 minutes until the solution became clear. The aldehyde (1.00 mmol) was then added and the mixture was heated under reflux. After 5 minutes, ethyl diazoacetate (2.00 mmol) was added in one portion and the reaction was stirred until the reaction reached completion as gauged by GC, ^{1}H NMR or TLC analysis. The mixture was cooled first to rt, then to -78 °C. $Pd_2(dba)_3$ (5 mg, 0.005 mmol) was added and a freshly prepared solution of diazomethane was slowly added (about 0.2 mL/min) until the reaction was completed. The conversion of the reaction was monitored either by NMR ^{1}H or by GC/MS. The solvent was removed under reduced pressure and the crude cyclopropane was purified by flash chromatography on silica gel.

Method B: Catalytic one-pot process in toluene.
CuI (10 mg, 0.050 mmol) and triphenylphosphine (262 mg, 1.00 mmol) were placed in a vessel which was backfilled with argon. Toluene (4.0 mL) was added and the resulting solution was stirred for 5 minutes until the solution became clear. The aldehyde (1.00 mmol) was then added and the mixture was heated at 80 °C. After 5 minutes, ethyl diazoacetate (2.00 mmol) was added in one portion and the reaction was stirred until the reaction reached completion as gauged by GC, ^{1}H NMR or TLC analysis. The mixture was cooled first to rt then to -78 °C. $Pd(OAc)_2$ (2 mg, 0.01 mmol) was added and a freshly prepared solution of diazomethane was slowly added (about 0.2 mL/min) until the reaction was completed. The conversion of the reaction was monitored either by NMR ^{1}H or by GC/MS. The solvent was removed under reduced pressure and the crude cyclopropane was purified by flash chromatography on silica gel.

Method C: Catalytic one-pot process in dichloroethane.
CuI (10 mg, 0.050 mmol) and triphenylphosphine (262 mg, 1.00 mmol) were placed in a vessel which was backfilled with argon. Dichloroethane (4 mL) was added and the resulting solution was stirred for 5 minutes until the solution became clear. The aldehyde (1.00 mmol) was then added and the mixture is heated at 80 °C. After 5 minutes, ethyl diazoacetate (2.00 mmol) was added in one portion and the reaction was stirred until the reaction reached completion as gauged by GC, ^{1}H NMR or TLC analysis. The mixture was first to rt, then to -78 °C. $Pd_2(dba)_3$ (5 mg, 0.005 mmol) was added and a freshly prepared solution of diazomethane was slowly added (about 0.2 mL/min) until the reaction was completed. The conversion of the reaction was monitored either by NMR ^{1}H or by GC/MS. The solvent was removed under reduced pressure and the crude cyclopropane was purified by flash chromatography on silica gel.

CHARACTERIZATION OF PRODUCTS



1

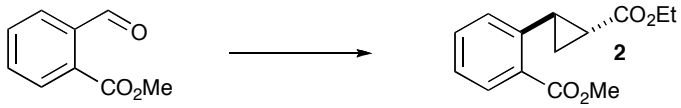
(1*R,2*R**)-Ethyl 2-phenylcyclopropanecarboxylate (1).**[9] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **1** (161 mg, 85%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.24 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.17 (M, 3H), 7.11-7.09 (M, 2H), 4.17 (q, J = 7 Hz, 2H), 2.55-2.48 (m, 1H), 1.93-1.87 (m, 1H), 1.63-1.57 (m, 1H), 1.34-1.27 (m, 1H), 1.28 (t, J = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3,

[9] Huang, L.; Chen, Y.; Gao, G.-Y.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 8179 - 8184.

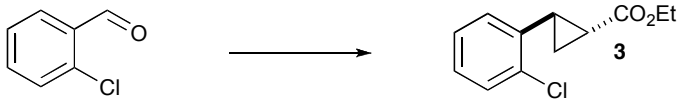
140.0, 128.4, 126.4, 126.1, 60.6, 26.1, 24.1, 17.0, 14.2. IR (neat) 3060, 1662, 1600, 1283, 1223, 1012 cm^{-1}.

(1*R,2*R**)-Ethyl 2-phenylcyclopropanecarboxylate (1).** The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 6.00 mmol of diazomethane. The desired cyclopropane **1** (131 mg, 69%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes).

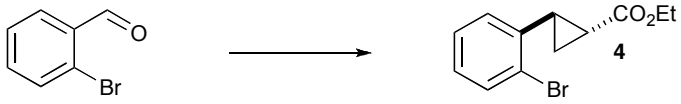
(1*R,2*R**)-Ethyl 2-phenylcyclopropanecarboxylate (1).** The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **C** using 6.00 mmol of diazomethane. The desired cyclopropane **1** (146 mg, 77%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes).



Methyl 2-((1*R,2*R**)-2-(ethoxycarbonyl)cyclopropyl)benzoate (2).** The title compound was prepared from methyl 2-formylbenzoate[10] (164 mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **2** (221 mg, 89%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.20 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8, 1 Hz, 1H), 7.44-7.40 (m, 1H), 7.30-7.26 (m, 1H), 7.13 (d, *J* = 8 Hz, 1H), 4.20 (q, *J* = 7 Hz, 2H), 3.88 (s, 3H), 3.14-3.09 (m, 1H), 1.78-1.73 (m, 1H), 1.63-1.58 (m, 1H), 1.36-1.31 (m, 1H), 1.30 (t, *J* = 7 Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 167.9, 140.5, 131.9, 131.4, 130.5, 127.2, 126.6, 60.5, 52.1, 25.4, 23.3, 15.6, 14.3; IR (neat) 2955, 1726, 1451, 1295, 1260, 1184 cm^{-1}; HRMS (FAB) calcd for $C_{14}H_{17}O_4$ $[M+H]^+$: 249.1121. Found 249.1120.



(1*R,2*R**)-Ethyl 2-(2-chlorophenyl)cyclopropanecarboxylate (3).**[11] The title compound was prepared from 2-chlorobenzaldehyde (113 μL, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **3** (157 mg, 70%) was obtained as a light yellow oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.25 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.35 (m, 1H), 7.19-7.15 (m, 2H), 7.02-6.99 (m, 1H), 4.20 (q, *J* = 7 Hz, 2H), 2.78-2.71 (m, 1H), 1.84-1.78 (m, 1H), 1.65-1.59 (m, 1H), 1.35-1.28 (m, 1H), 1.29 (t, *J* = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 137.4, 135.6, 129.3, 127.8, 127.0, 126.7, 60.7, 24.2, 22.9, 15.5, 14.2; IR (neat) 2981, 1726, 1445, 1408, 1326, 1182 cm^{-1}.

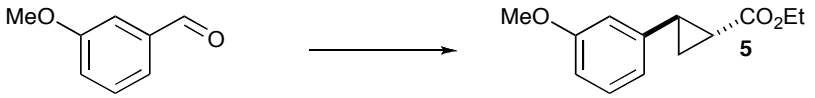


(1*R,2*R**)-Ethyl 2-(2-bromophenyl)cyclopropanecarboxylate (4).** The title compound was prepared from 2-bromobenzaldehyde (117 μL, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **4** (180 mg, 67%) was obtained as a light yellow oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.27 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 8, 1 Hz, 1H), 7.26-7.20 (m, 1H), 7.11-7.00 (m, 2H), 4.21 (q, J = 7 Hz, 2H), 2.74-2.67 (m, 1H), 1.82-1.76 (m, 1H), 1.65-1.59 (m, 1H), 1.36-1.28 (m, 1H), 1.29 (t, *J* = 7 Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 139.0, 132.5, 128.1, 127.4, 127.3, 126.2, 60.7, 26.9, 23.1, 15.6,

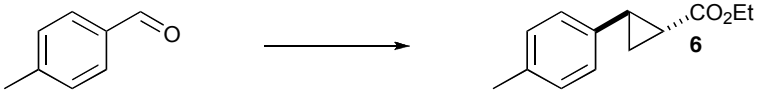
[10] This compound was prepared from 2-carboxybenzaldehyde: Ye, B.-H.; Naruta, Y. *Tetrahedron*, **2003**, *59*, 3593-3601.

[11] Kaiser, C.; Lester, B. M.; Zirkle, C. L.; Burger, A.; Davis, C. S.; Delia, T. J.; Zirngibl, L. *J Med. Chem*. **1962**, *5*, 1243-65.

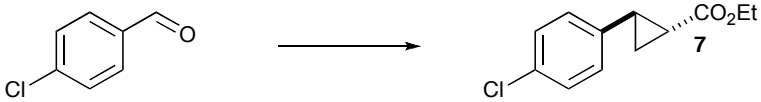
14.3. IR (neat) 2980, 1725, 1444, 1407, 1324, 1181 cm^{-1} ; HRMS (FAB) calcd for $C_{12}H_{14}BrO_2$ $[M+H]^+$: 269.0171. Found 269.0175.



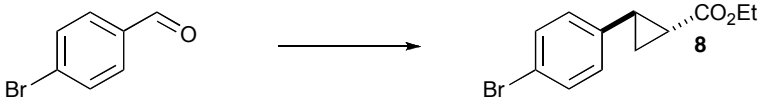
(1*R,2*R**)-Ethyl 2-(3-methoxyphenyl)cyclopropanecarboxylate (5).**[12] The title compound was prepared from *m*-anisaldehyde (122 μL, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **5** (202 mg, 92%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.46 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 8 Hz, 1H), 6.74 (d, *J* = 8 Hz, 1H), 6.68 (d, *J* = 8 Hz, 1H), 6.64 (s, 1H), 4.16 (q, *J* = 7 Hz, 2H), 3.79 (s, 3H), 2.51-2.46 (m, 1H), 1.92-1.87 (m, 1H), 1.61-1.56 (m, 1H), 1.32-1.27 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 159.6, 141.7, 129.4, 118.4, 112.0, 111.6, 60.7, 55.1, 26.1, 24.1, 17.0, 14.2; IR (neat) 2980, 2835, 1722, 1603, 1407, 1181 cm^{-1}; HRMS (FAB) calcd for $C_{13}H_{17}O_3$ $[M+H]^+$: 221.1168. Found 221.1172.



(1*R,2*R**)-Ethyl 2-*p*-tolylcyclopropanecarboxylate (6).**[9] The title compound was prepared from *p*-tolualdehyde (118 μL, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **6** (163 mg, 80%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.18 (5% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8 Hz, 2H), 6.99 (d, *J* = 8 Hz, 2H), 4.16 (q, *J* = 7 Hz, 2H), 2.52-2.45 (m, 1H), 2.31 (s, 3H), 1.89-1.83 (m, 1H), 1.60-1.53 (m, 1H), 1.31-1.14 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 137.0, 136.0, 129.1, 126.0, 60.6, 25.9, 24.0, 20.9, 16.9, 14.2; IR (neat) 2981, 1725, 1405, 1331, 1182 cm^{-1}.



(1*R,2*R**)-Ethyl 2-(4-chlorophenyl)cyclopropanecarboxylate (7).**[13] The title compound was prepared from 4-chlorobenzaldehyde (140 mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **7** (169 mg, 75%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.32 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8 Hz, 2H), 7.02 (d, *J* = 8 Hz, 2H), 4.17 (q, *J* = 7 Hz, 2H), 2.50-2.45 (m, 1H), 1.88-1.83 (m, 1H), 1.62-1.57 (m, 1H), 1.29-1.24 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 138.6, 132.1, 128.5, 127.5, 60.7, 25.4, 24.1, 17.0, 14.2; IR (neat) 2981, 1722, 1496, 1328, 1185 cm^{-1}.

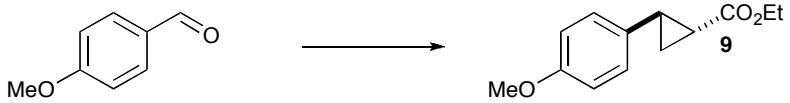


(1*R,2*R**)-Ethyl 2-(4-bromophenyl)cyclopropanecarboxylate (8).**[12] The title compound was prepared from 4-bromobenzaldehyde (185 mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **8** (193 mg, 72%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.35 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8 Hz, 2H), 6.96 (d, *J* = 8 Hz, 2H), 4.16 (q, *J* = 7 Hz, 2H), 2.50-2.43 (m, 1H),

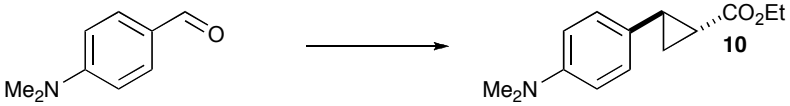
12 Hixson, S. S.; Franke, L. A.; Gere, J. A.; Xing, Y. D. *J. Am. Chem. Soc.* **1988**, *110*, 3601-10.

13 Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Adv. Synth. Catal.* **2001**, *343*, 79-88.

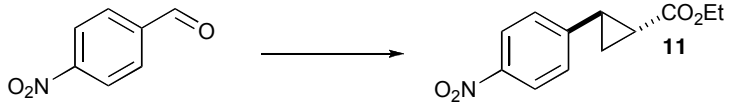
1.89-1.83 (m, 1H), 1.63-1.56 (m, 1H), 1.29-1.23 (m, 1H), 1.27 (t, J = 7Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 139.1, 131.4, 127.8, 120.1, 60.8, 25.5, 24.1, 17.0, 14.2; IR (neat) 2984, 1720, 1495, 1408, 1328, 1183 cm^{-1}.



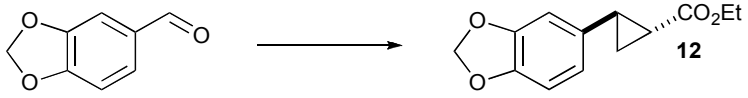
(1*R,2*R**)-Ethyl 2-(4-methoxyphenyl)cyclopropanecarboxylate (9).**[9] The title compound was prepared from *p*-anisaldehyde (121 μL, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **9** (168 mg, 76%) was obtained as a light yellow solid after flash chromatography (10% EtOAc/Hexanes). R_f 0.38 (20% EtOAc/hexanes). M.p. 83 °C (litt. 85 °C).[14] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (d, J = 8 Hz, 2H), 6.82 (d, J = 8 Hz, 2H), 4.16 (q, J = 7 Hz, 2H), 3.78 (s, 3H), 2.51-2.44 (m, 1H), 1.85-1.79 (m, 1H), 1.58-1.52 (m, 1H), 1.28-1.22 (m, 1H), 1.27 (t, J = 7Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 158.2, 132.0, 127.3, 113.8, 60.6, 55.2, 25.6, 23.8, 16.7, 14.2. IR (neat) 2982, 1721, 1606, 1408, 1180 cm^{-1}.



(1*R,2*R**)-Ethyl 2-(4-(dimethylamino)phenyl)cyclopropanecarboxylate (10).** The title compound was prepared from 4-dimethylaminobenzaldehyde (149 mg, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **10** (147 mg, 63%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.34 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J = 8 Hz, 2H), 6.67 (d, J = 8 Hz, 2H), 4.15 (q, J = 7 Hz, 2H), 2.91 (s, 6H), 2.47-2.42 (m, 1H), 1.82-1.77 (m, 1H), 1.54-1.50 (m, 1H), 1.27-1.22 (m, 1H), 1.27 (t, J = 7Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 149.4, 127.8, 127.0, 112.8, 60.5, 40.7, 25.7, 23.7, 16.5, 14.2; IR (neat) 2979, 2903, 1713, 1520, 1335, 1176 cm^{-1}; HRMS (FAB) calcd for $C_{14}H_{20}NO_2$ $[M+H]^+$: 234.1483. Found 234.1488.



(1*R,2*R**)-Ethyl 2-(4-nitrophenyl)cyclopropanecarboxylate (11).**[15] The title compound was prepared from 4-nitrobenzaldehyde (151 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **11** (139 mg, 59%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.45 (20% EtOAc/hexanes); m.p. 52 °C (litt.: 50 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J = 9 Hz, 2H), 7.20 (d, J = 9 Hz, 2H), 4.18 (q, J = 7 Hz, 2H), 2.62-2.56 (m, 1H), 2.02-1.96 (m, 1H), 1.75-1.69 (m, 1H), 1.41-1.34 (m, 1H), 1.28 (t, J = 7Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 148.1, 146.5, 126.6, 123.7, 61.0, 25.6, 25.1, 17.8, 14.2; IR (neat) 2982, 1721,1517, 1343, 1177 cm^{-1}.



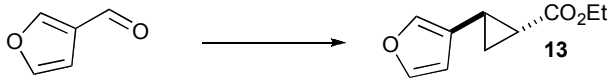
(1*R,2*R**)-Ethyl 2-(benzo[d][1,3]dioxol-6-yl)cyclopropanecarboxylate (12).**[16] The title compound was prepared from piperonal (150 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **12** (171 mg, 73%) was obtained as a light yellow oil

[14] Herbert O. House, H.O.; McDaniel, W. C.; Sieloff, R. F.;Vanderveer D. *J. Org. Chem.* **1978**, *43*, 4316-4323.

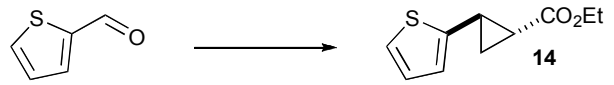
[15] Rasmussen, T.; Jensen, J. F.; Oestergaard, N.; Tanner, D.; Ziegler, T.; Norrby, P.-O. *Chem. Eur. J.* **2002**, *8*, 177-184.

[16] Yamashita, M.; Okuyama, K.; Ohhara, T.; Kawasaki, I.; Sakai, K. *Chem. Pharm. Bull.* **1995**, *43*, 2075-2081.

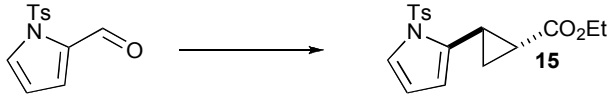
after flash chromatography (10% EtOAc/Hexanes). R_f 0.40 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (d, *J* = 10 Hz, 1H), 6.60 (dd, *J* = 10, 2 Hz, 1H), 6.56 (d, *J* = 2 Hz, 1H), 5.91 (s, 2H), 4.16 (q, *J* = 10 Hz, 2H), 2.48-2.42 (m, 1H), 1.83-1.77 (m, 1H), 1.56-1.50 (m, 1H), 1.27 (t, *J* = 10 Hz, 3H) 1.26-1.19 (m, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 147.7, 146.1, 133.8, 119.6, 108.1, 106.6, 100.9, 60.6, 26.0, 23.9, 16.7, 14.2; IR (neat) 2890, 1487, 1245, 1039 cm^{-1}.



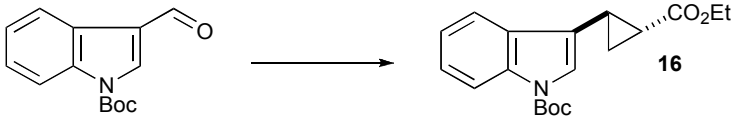
(1*R,2*R**)-Ethyl 2-(furan-3-yl)cyclopropanecarboxylate (13).** The title compound was prepared from 3-furfuraldehyde (86 μL mg, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **13** (128 mg, 71%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.15 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.28 (s, 1H), 6.15 (s, 1H), 4.15 (q, *J* = 7 Hz, 2H), 2.35-2.30 (m, 1H), 1.77-1.73 (m, 1H), 1.51-1.47 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H) 1.14-1.09 (m, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 143.1, 139.1, 124.7, 108.9, 60.6, 22.6, 17.1, 16.1, 14.2; IR (neat) 2981, 2933, 1721, 1323, 1181 cm^{-1}; HRMS (FAB) calcd for $C_{10}H_{13}O_3$ $[M+H]^+$: 181.0865. Found 181.0866.



(1*R,2*R**)-Ethyl 2-(thiophen-2-yl)cyclopropanecarboxylate (14).**[16] The title compound was prepared from 2-thiophenecarboxaldehyde (93 μL, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **14** (125 mg, 77%) was obtained as colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.35 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 5 Hz, 1H), 6.90 (dd, *J* = 5, 4 Hz, 1H), 6.82 (d, *J* = 4 Hz, 1H), 4.17 (q, *J* = 7 Hz, 2H), 2.72-2.67 (m, 1H), 1.95-1.90 (m, 1H), 1.64-1.59 (m, 1H), 1.34-1.28 (m, 1H), 1.28 (t, *J* = 7 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 144.1, 126.8, 123.8, 123.0, 60.7, 24.9, 21.4, 17.9, 14.2; IR (neat) 2980, 1721, 1404, 1178, 1045 cm^{-1}.



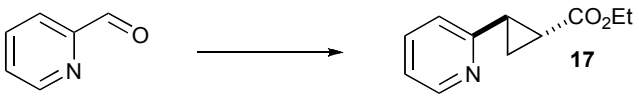
(1*R,2*R**)-Ethyl 2-(1-tosyl-1H-pyrrol-2-yl)cyclopropanecarboxylate (15).** The title compound was prepared from 1-tosyl-1H-pyrrole-2-carbaldehyde[17] (249 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **15** (273 mg, 82%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.29 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8 Hz, 2H), 7.26-7.21 (m, 3H), 6.10 (t, *J* = 3Hz, 1H), 5.83 (s, 1H), 4.15 (q, *J* = 7 Hz, 2H), 2.57-2.52 (m, 1H), 2.36 (s, 3H), 1.58-1.54 (m, 1H), 1.39-1.33 (m, 1H), 1.26 (t, *J* = 7 Hz, 3H), 1.06-1.01 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 144.8, 136.1, 133.6, 129.9, 127.0, 122.9, 111.3, 110.7, 60.7, 23.3, 21.6, 18.2, 15.1, 14.2; IR (neat) 2981, 2923, 1721, 1366, 1175, 1154, 1055 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{20}NO_4S$ $[M+H]^+$: 334.1107. Found 334.1101.



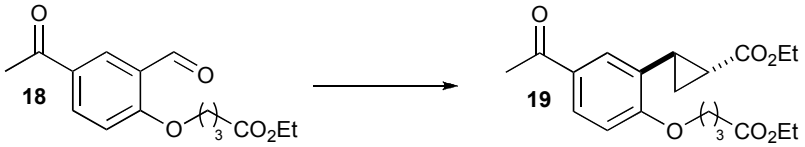
***tert*-Butyl 3-(1*R**,2*R**)-2-(ethoxycarbonyl)cyclopropyl)-1H-indole-1-carboxylate (16).** The title compound was prepared from *tert*-butyl 3-formyl-1H-indole-1-carboxylate[18] (245 mg, 1.00 mmol)

[17] Masquelin, T.; Broger, E.; Mueller, K.; Schmid, R.; Obrecht, D. *Helv. Chim. Acta*, **1994**, *77*, 1395-1411.
[18] Davies, J. R.; Kane, P. D.; Moody, C. J.; Slawin, A. M. Z. *J. Org. Chem.* **2005**, *70*, 5840-5851.

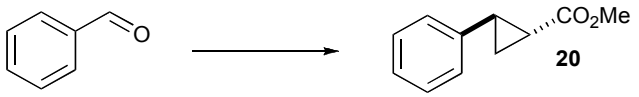
according to the general procedure **A** using 10.50 mmol of diazomethane. The desired cyclopropane **16** (227 mg, 69%) was obtained as a light yellow oil after an oxidative work-up and a flash chromatography (5% EtOAc/Hexanes). R_f 0.43 (20% EtOAc/hexanes). The oxidative work-up proceeded as follow: The crude product was dissolved in dichloromethane (10 mL) and cooled to −78°C. The solution was treated with ozone until the solution was blue. Oxygen was then bubbled into the mixture until the blue color had disappeared. Methyl sulfide (1 mL) was added at −78°C and left to warm to room temperature overnight. The solution was concentrated under reduced pressure and the residue was purified by column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 7 Hz, 1H), 7.61 (d, J = 8 Hz, 1H), 7.35-7.23 (m, 3H), 4.21 (q, J = 7 Hz, 2H), 2.57-2.50 (m, 1H), 1.92-1.87 (m, 1H), 1.66 (s, 9H), 1.62-1.55 (m, 2H), 1.31 (t, J = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 149.5, 135.4, 130.4, 124.6, 122.5, 121.9, 120.2, 118.9, 115.2, 83.6, 60.7, 28.1, 21.7, 17.1, 15.3, 14.2. IR (neat) 2976, 1743, 1365, 1150 cm^{-1}; HRMS (FAB) calcd for $C_{19}H_{24}NO_4$ $[M+H]^+$: 330.1699. Found 330.1695.



(1*R,2*R**)-Ethyl 2-(pyridin-2-yl)cyclopropanecarboxylate (17).**[10] The title compound was prepared from 2-pyridinecarboxaldehyde (95 μL mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **17** (117 mg, 61%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.25 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43-8.41 (m, 1H), 7.56-7.50 (m, 1H), 7.20 (d, J = 8 Hz, 1H), 7.08-7.03 (m, 1H), 4.14 (q, J = 7 Hz, 2H), 2.59-2.52 (m, 1H), 2.25-2.19 (m, 1H), 1.63-1.54 (m, 2H), 1.25 (t, J = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 158.8, 149.3, 135.9, 122.4, 121.2, 60.6, 27.1, 24.2, 17.2, 14.1; IR (neat) 2981, 1721, 1595, 1475, 1329, 1178 cm^{-1}.



(1*R,2*R**)-Ethyl 2-(2-(3-(ethoxycarbonyl)propoxy)-5-acetylphenyl) cyclopropanecarboxylate (19).** The title compound was prepared from ethyl 4-(4-acetyl-2-formylphenoxy)butanoate **18**[19] (278 mg, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropanes **19** (188 mg, 52%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.43 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 12, 3 Hz, 1H), 7.58 (d, J = 3 Hz, 1H), 6.84 (d, J = 12 Hz, 1H), 4.23-4.08 (m, 6H), 2.68-2.61 (m, 1H), 2.52 (s, 3H), 2.51 (t, J = 10 Hz, 2H), 2.19-2.10 (m, 2H), 1.81-1.75 (m, 1H), 1.59-1.53 (m, 1H), 1.40-1.33 (m, 1H), 1.28 (t, J = 10 Hz, 3H), 1.24 (t, J = 10 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 173.5, 172.9, 161.5, 129.8, 129.2, 128.6, 126.7, 110.1, 67.1, 60.6, 60.4, 30.4, 26.2, 24.4, 22.4, 21.2, 14.9, 14.2, 14.1. IR (neat) 2980, 1725, 1676, 1601, 1259, 1182; HRMS (FAB) calcd for $C_{20}H_{27}O_6$ $[M+H]^+$: 363.1802. Found 363.1812.

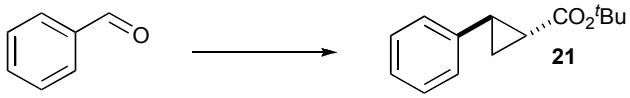


(1*R,2*R**)-Methyl 2-phenylcyclopropanecarboxylate (20).**[20] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **20** (143 mg, 81%) was obtained as a colorless oil after flash

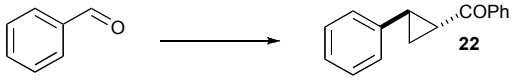
[19] Kahnberg, P.; Lee, C. W.; Grubbs, R. H.; Sterner, O. *Tetrahedron* **2002**, *58*, 5203-5208.

[20] Walser, P.; Renold, P.; N'Goka, V.; Hosseinzadeh, F.; Tamm, C. *Helv. Chim. Acta* **1991**, *74*, 1941-1952.

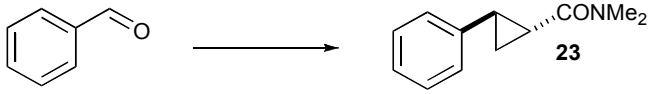
chromatography (5% EtOAc/Hexanes). R_f 0.29 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.22-7.20 (m, 1H), 7.11-7.09 (m, 2H), 3.72 (s, 3H), 2.56-2.51 (m, 1H), 1.93-1.89 (m, 1H), 1.63-1.58 (m, 1H), 1.35-1.30 (m, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 139.9, 128.4, 126.4, 126.1, 51.8, 26.2, 23.9, 16.9; IR (neat) 3029, 2951, 1724, 1440, 1197, 1171 cm^{-1}.



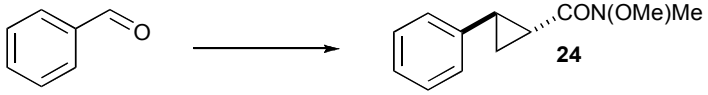
(1*R,2*R**)-*tert*-Butyl 2-phenylcyclopropanecarboxylate (21).**[21] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **C** using 6.00 mmol of diazomethane. The desired cyclopropane **21** (161 mg, 74%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.34 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.21-7.17 (m, 1H), 7.10-7.08 (m, 2H), 2.46-2.41 (m, 1H), 1.85-1.81 (m, 1H), 1.55-1.50 (m, 1H), 1.46 (s, 9H), 1.25-1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 140.5, 128.4, 126.2, 126.0, 80.5, 28.1, 25.7, 25.2, 17.0; IR (neat) 2977, 1705, 1637, 1328, 1314, 1148 cm^{-1}.



Phenyl((1*R,2*R**)-2-phenylcyclopropyl)methanone (22).**[22] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 6.00 mmol of diazomethane. The desired cyclopropane **22** (162 mg, 73%) was obtained as a yellow solid after flash chromatography (5% EtOAc/Hexanes). R_f 0.53 (20% EtOAc/hexanes); m.p. 44 °C (litt. 45-47 °C);[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7 Hz, 2H), 7.58-7.54 (m, 1H), 7.48-7.44 (m, 2H), 7.33-7.30 (m, 2H), 7.26-7.17 (m, 3H), 2.93-2.89 (m, 1H), 2.73-2.68 (m, 1H), 1.95-1.91 (m, 1H), 1.59-1.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 140.4, 137.7, 132.8, 128.5 (2C), 128.0, 126.5, 126.2, 29.9, 29.2, 19.2; IR (neat) 2980, 1711, 1627, 1272, 1164 cm^{-1}.



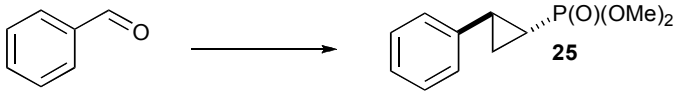
(1*R,2*R**)-*N*,*N*-dimethyl-2-phenylcyclopropanecarboxamide (23).**[24] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 4.50 mmol of diazomethane. The desired cyclopropane **23** (155 mg, 82%) was obtained as a colorless solid after flash chromatography (50% EtOAc/Hexanes). R_f 0.19 (50% EtOAc/hexanes); m.p. 59 °C (litt. 61 °C);[10] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.12 (m, 5H), 3.14 (s, 3H), 3.00 (s, 3H), 2.52-2.45 (m, 1H), 2.03-1.97 (m, 1H), 1.68-1.61 (m, 1H), 1.30-1.24 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 141.0, 128.4, 126.1, 126.0, 37.2, 35.8, 25.4, 23.1, 16.2.; IR (neat) 3028, 2930, 1634, 1496, 1417, 1139 cm^{-1}.



(1*R,2*R**)-*N*-methoxy-*N*-methyl-2-phenylcyclopropanecarboxamide (24).**[25] The title compound was prepared from benzaldehyde (102μL, 1.00 mmol) according to the general procedure **C** using 4.50 mmol of diazomethane. The desired cyclopropane **24** (181 mg, 88%) was obtained as a pale yellow oil after flash chromatography (50% EtOAc/Hexanes). R_f 0.22 (80% EtOAc/hexanes). M.p. 59 °C. ^{1}H

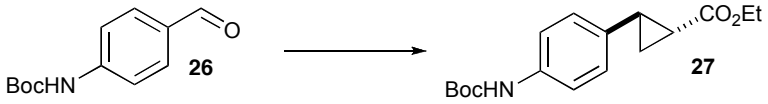
[21] Lyle, M. P. A.; Wilson, P. D. *Org. Lett.* **2004**, *6*, 855-858.
[22] Pyne, S. G.; Dong, Z.; Skelton, B. W.; White, A. H. *J. Org. Chem.* **1997**, *62*, 2337-2343.
[23] Wessig, P.; Muhling, O. *Helv. Chim. Acta*, **2003**, *86*, 865-893.
[24] Doyle, M. P.; Loh, K.-L.; DeVries, K. M.; Chinn, M. S. *Tetrahedron Lett.* **1987**, *28*, 833-836.
[25] Woo, J. C. S.; Fenster, E.; Dake, G. R. *J. Org. Chem.* **2004**, *69*, 8984-8986.

NMR (300 MHz, $CDCl_3$) δ 7.30-7.12 (m, 5H), 3.69 (s, 3H), 3.23 (s, 3H), 2.53-2.39 (m, 2H), 1.66-1.60 (m, 1H), 1.34-1.27 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 140.7, 128.4, 126.26, 126.20, 61.7, 32.5, 25.9, 21.5, 16.5; IR (neat) 2936, 2241, 1650, 1437, 1274, 1176, 1119, 995, 910, 728 cm^{-1}.

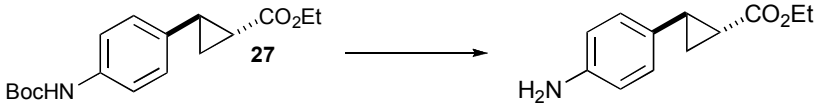


(1*R,2*R**)-Dimethyl 2-phenylcyclopropylphosphonate (25).**[26] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 4.50 mmol of diazomethane. The desired cyclopropane **25** (156 mg, 69%) was obtained as a yellow oil after flash chromatography (80% EtOAc/Hexanes). R_f 0.31 (100% EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.22-7.18 (m, 1H), 7.11 (d, *J* = 7 Hz, 2H), 3.79 (d, *J* = 8 Hz, 3H), 3.76 (d, *J* = 8 Hz, 3H), 2.53-2.44 (m, 1H), 1.54-1.45 (m, 1H), 1.30-1.22 (m, 1H), 1.16-1.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8 (d, *J* = 3 Hz), 128.5, 126.6, 126.1, 52.7 (d, *J* = 8 Hz), 20.9 (d, *J* = 5 Hz), 13.8 (d, *J* = 192 Hz), 12.4 (d, *J* = 6 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 23.1; IR (neat) 2952, 2851, 1459, 1244, 1027 cm^{-1}.

SYNTHESIS OF CYCLOPROPANECARBOXYLIC ACID 31.



***tert*-Butyl 4-((1*R**,2*R**)-2-(ethoxycarbonyl)cyclopropyl)phenylcarbamate (27).** The title compound was prepared from 4-(*tert*-butoxycarbonylamino)benzaldehyde (**26**)[27] (221 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **27** (256 mg, 84%) was obtained as a colorless oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.26 (20% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8 Hz, 2H), 7.01 (d, *J* = 8 Hz, 2H), 6.44 (s(br), 1H), 4.15 (q, *J* = 7 Hz, 2H), 2.49-2.44 (m, 1H), 1.85-1.80 (m, 1H), 1.57-1.53 (m, 1H), 1.50 (s, 9H), 1.29-1.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 152.6, 136.7, 134.6, 126.7, 118.6, 80.4, 60.6, 28.3, 25.7, 23.9, 16.8, 14.2; IR (neat) 3265, 2974, 1728, 1518, 1155 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{23}NO_4Na$ $[M+Na]^+$: 328.1519. Found 328.1514.



(1*R,2*R**)-Ethyl 2-(4-aminophenyl)cyclopropanecarboxylate.** To a solution of **27** (200 mg, 0.65 mmol) in DCM (4 mL) at 0 °C, was added TFA (2 mL). The resulting mixure was warmed at RT and stirred for 2 hours. The mixture was diluted with DCM (10 mL) then washed with 10% aqueous K_2CO_3 (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% MeOH/DCM). R_f 0.32 (20% MeOH/DCM). The free amine was obtained as a yellow oil (113 mg, 85%). ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, *J* = 9 Hz, 2H), 6.60 (d, *J* = 9 Hz, 2H), 4.15 (q, *J* = 7 Hz, 2H), 3.60 (s (br), 2H), 2.45-2.40 (m, 1H), 1.81-1.76 (m, 1H), 1.54-1.49 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H), 1.25-1.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 144.9, 129.8, 127.2, 115.1, 60.5, 25.8, 23.7, 16.5, 14.2; IR (neat) 3352, 2943, 1679, 1501, 1247 cm^{-1}; HRMS (FAB) calcd for $C_{12}H_{16}NO_2$ $[M+H]^+$: 206.1175. Found 206.1174.

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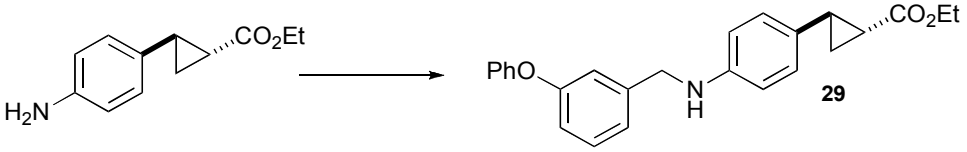
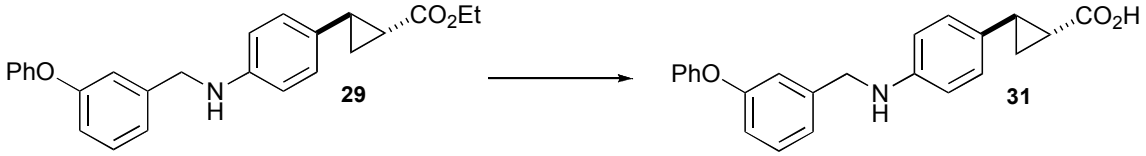
[26] Charette, A.B.C.; Bouchard, J.-E. *Can. J. Chem.* **2005**, *83*, 533-542.

[27] Niimi, T.; Orita, M.; Okazawa-Igarashi, M.; Sakashita, H.; Kikuchi, K.; Ball, E.; Ichikawa, A.; Yamagiwa, Y.; Sakamoto, S.; Tanaka, A.; Tsukamoto, S.; Fujita, S.; Tatsuta, K.; Maeda, Y.; Chikauchi, K. *J. Med. Chem.* **2001**, *44*, 4737-4740.

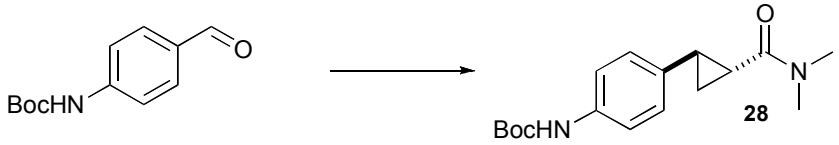


(1*R,2*R**)-Ethyl 2-(4-(3-phenoxybenzylamino)phenyl)cyclopropanecarboxylate (29).** A mixture of (1*R**,2*R**)-ethyl 2-(4-aminophenyl)cyclopropanecarboxylate (80 mg, 0.39 mmol) and 3-(phenyloxy)benzaldehyde (93 mg, 0.47 mmol) in DCE (4 mL) was heated at 80 °C for 2 hours then cooled to RT. Acetic acid (1 drop) and $NaHB(OAc)_3$ (123 mg, 0.58 mmol) were added and the reaction was stirred until the reaction was completed by TLC analysis. The mixture was diluted with DCM (10 mL) and washed with water (20 mL), dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (25% EtOAc/hexane). R_f 0.44 (50% EtOAc/hexane). The desired product was obtained as a yellow oil (117 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.28 (m, 3H), 7.12-6.87 (m, 8H), 6.53 (d, *J* = 8 Hz, 2H), 4.29 (s, 2H), 4.15 (q, *J* = 7 Hz, 2H), 4.02 (br, 1H), 2.46-2.39 (m, 1H), 1.80-1.75 (m, 1H), 1.54-1.48 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H), 1.25-1.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 157.5, 156.9, 146.5, 141.5, 129.8, 129.7, 128.8, 127.2, 123.2, 122.0, 118.9, 117.6, 117.4, 112.9, 60.5, 48.0, 25.8, 23.7, 16.5, 14.2; IR (neat) 2930, 1685, 1494, 1255 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{26}NO_3$ $[M+H]^+$: 388.1899. Found 388.1907.



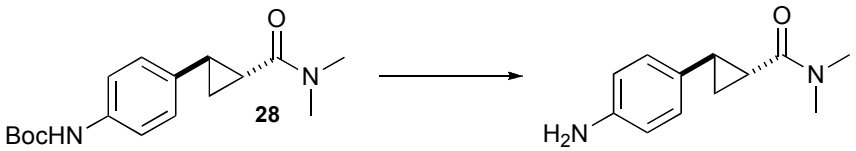
(1*R,2*R**)-2-(4-(3-Phenoxybenzylamino)phenyl)cyclopropanecarboxylic acid (31).** To solution of **29** (90 mg, 0.23 mmol) in MeOH (10 mL), was added a 25% aqueous NaOH solution (1 mL). The resulting mixture was heated under reflux overnight. The solution was diluted with water (5 mL) and the pH was adjusted to 3-4 with a saturated $NaHSO_3$ solution. The mixture was washed with DCM (10 mL) and the organic layer was dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (10% MeOH/DCM). R_f 0.29 (20% MeOH/DCM). The desired product **31** was obtained as a gum (77 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 3H), 7.12-7.01 (m, 2H), 7.01-6.98 (m, 3H), 6.94-6.88 (m, 3H), 6.54 (d, *J* = 9 Hz, 2H), 4.29 (s, 2H), 2.54-2.49 (m, 1H), 1.80-1.76 (m, 1H), 1.60-1.56 (m, 1H), 1.35-1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6, 157.5, 156.9, 146.7, 141.4, 129.9, 129.7, 128.3, 127.3, 123.2, 122.0, 118.9, 117.6, 117.4, 112.9, 48.0, 26.8, 23.5, 17.0; IR (neat) 2922, 1691, 1488, 1248, 1218, 735 cm^{-1}; HRMS (FAB) calcd for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1585. Found 360.1594.

SYNTHESIS OF CYCLOPROPANECARBOXAMIDE 30.

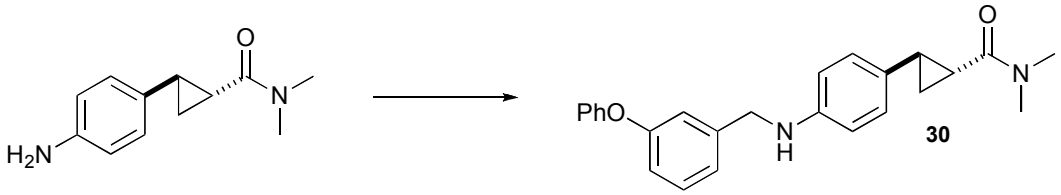


***tert*-Butyl 4-(*(1R*,2R*)*-2-(dimethylcarbamoyl)cyclopropyl)phenylcarbamate (28).** The title compound was prepared from 4-(*tert*-butoxycarbonylamino)benzaldehyde[27] according to the general procedure **C** using 9.00 mmol of diazomethane. The desired cyclopropane **28** (219 mg, 72%) was obtained as a colorless oil after flash chromatography (50% EtOAc/hexane). R_f 0.15 (10% EtOAc/DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9 Hz, 2H), 7.03 (d, *J* = 9 Hz, 2H), 6.47 (br, 1H), 3.11 (s, 3H), 2.98 (s, 3H), 2.45-2.38 (m, 1H), 1.94-1.88 (m, 1H), 1.63-1.57 (m, 1H), 1.50 (s, 9H), 1.25-1.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 152.6, 136.7, 134.6, 126.7, 118.6, 80.4, 60.6,

28.3, 25.7, 23.9, 16.8, 14.2; IR (neat) 3283, 2980, 1721, 1631, 1527, 1162 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{25}N_2O_3$ $[M+H]^+$: 304.1786. Found 304.1852.



(1*R,2*R**)-2-(4-aminophenyl)-*N,N*-dimethylcyclopropanecarboxamide.** To a solution of **28** (88 mg, 0.29 mmol) in DCM (2 mL) at 0 °C, was added TFA (1 mL). The resulting mixture was warmed at RT and stirred for 2 hours. The mixture was diluted with DCM (10 mL), then washed with 10% aqueous K_2CO_3 (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% MeOH/DCM). R_f 0.46 (20% MeOH/DCM). The free amine was obtained as a yellow oil (56 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (d, *J* = 8 Hz, 2H), 6.61 (d, *J* = 8 Hz, 2H), 3.58 (s (br), 2H), 3.12 (s, 3H), 2.98 (s, 3H), 2.41-2.35 (m, 1H), 1.90-1.84 (m, 1H), 1.58-1.52 (m, 1H), 1.20-1.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 144.6, 130.9, 127.1, 115.1, 37.2, 35.8, 25.0, 22.7, 15.6; IR (neat) 3341, 3228, 3006, 2929, 1622, 1519, 1285, 1141 cm^{-1}; HRMS (FAB) calcd for $C_{12}H_{17}N_2O$ $[M+H]^+$: 205.1337. Found 205.1340.



(1*R,2*R**)-2-(4-(3-phenoxybenzylamino)phenyl)-*N,N*-dimethylcyclopropanecarboxamide (30).** To a mixture of (1*R**,2*R**)-2-(4-aminophenyl)-*N,N*-dimethylcyclopropanecarboxamide (80 mg, 0.39 mmol), 3-(phenyloxy)benzaldehyde (93 mg, 0.47 mmol) and acetic acid (1 drop) in DCE (4 mL) was added $NaHB(OAc)_3$ (123 mg, 0.58 mmol). The reaction was stirred at RT until the reaction was completed by TLC analysis (2 hours). The mixture was diluted with DCM (10 mL) then washed with water (20 mL), dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (10% MeOH/DCM). R_f 0.32 (20% MeOH/DCM). The desired product **30** was obtained as a yellow oil (128 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.26 (m, 3H), 7.13-7.08 (m, 2H), 7.02-6.88 (m, 6H), 6.54 (d, *J* = 8 Hz, 2H), 4.28 (s, 2H), 4.05 (br, 1H), 3.11 (s, 3H), 2.98 (s, 3H), 2.40-2.35 (m, 1H), 1.89-1.85 (m, 1H), 1.58-1.53 (m, 1H), 1.20-1.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 157.5, 156.9, 146.3, 141.5, 129.9, 129.8, 129.7, 127.1, 123.2, 122.0, 118.8, 117.6, 117.4, 112.9, 48.1, 37.2, 35.8, 25.0, 22.6, 15.6; IR (neat) 3336, 2926, 1615, 1523, 1486, 1247 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{27}N_2O_2$ $[M+H]^+$: 387.2079. Found 387.2072.