

## Stereoselective construction of nitrile-substituted cyclopropanes

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Supporting Information

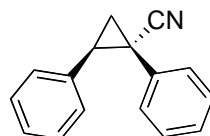
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## Experimental Details

2-Diazo-2-phenylethanenitrile (**5**) was synthesized from the corresponding literature procedure.<sup>1</sup> Dirhodium catalysts were synthesized from the procedures reported in the literature.<sup>2</sup> Rh<sub>2</sub>(S-DOSP)<sub>4</sub> and Rh<sub>2</sub>(S-PTAD)<sub>4</sub> and their enantiomers are commercially available from STREAM®.

**General Cyclopropanation Procedure:** To a flame dried round bottom flask under argon, equipped with a stir bar, was added toluene, the electron rich olefin (5.0 equiv.), and the Rh (II) catalyst (2 mol %). The green solution was then degassed by bubbling argon through the solution for 5 min. After degassing, the solution was then cooled to -78°C and the diazo compound solution (1.0 equiv. in toluene, ~0.1M) was then added drop wise over 15 min. The orange solution was then allowed to gradually warm to rt over 6 h. After which, the resulting green solution was then concentrated *in vacuo* and the dr was determined by <sup>1</sup>H NMR. The crude cyclopropane was then further purified by column chromatography and the ee was determined by chiral HPLC.



**(1S, 2R)- 1,2-Diphenylcyclopropanecarbonitrile (6a):** Cyclopropane **6a** was obtained as a white solid, purified by 15:1 to 9:1 hexanes to diethyl ether using SiO<sub>2</sub> gel.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.16-7.09 (m, 8H), 6.90-6.88 (m, 2H), 3.17 (t, *J* = 8.4Hz, 1H), 2.14-2.07 (m, 2H). <sup>1</sup>H NMR data were consistent with published data.<sup>3</sup>

ee 90% determined by chiral HPLC [OD, 1.0 mL/min, 0.8% isopropanol in hexanes, *t<sub>R</sub>*=23.1 min (major) and 35.0 min (minor) , UV 230nm].

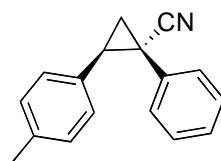
Nitrilecyclopropane **6a** was then recrystallized from dissolving in boiling hexanes following by cooling to room temperature to give crystals with ee >98% and a recovered yield of 85%.

[α]<sub>D</sub><sup>25</sup> = +80.5 (*c* = 0.50, CHCl<sub>3</sub>). [ee >98%]

<sup>1</sup> Breslow, R.; Yuan, C. *J. Am. Chem. Soc.*, 1958, **80**, 5991.

<sup>2</sup> R. Reddy, G. Lee, and H. M. L. Davies, *Org. Lett.*, 2006, **8**, 3437; T. Takahashi, H. Tsutsui, M. Tamura, S. Kitagaki, M. Nakajima, and S. Hashimoto, *Chem. Commun.*, 2001, 1604; Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.*, 1996, **118**, 6897.

<sup>3</sup> Doering, W. E.; Robertson, L. R.; Ewing, E. E. *J. Org. Chem.*, 1983, **48**, 4280.



**(1S, 2R)- 1-Phenyl-2-p-tolylcyclopropanecarbonitrile (6b):** Cyclopropane **6b** was obtained as a white solid, purified by 15:1 to 9:1 hexanes to diethyl ether using SiO<sub>2</sub> gel. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.16-7.08 (m, 5H), 6.89 (d, *J* = 8.0Hz, 2H), 6.76 (d, *J* = 8.0Hz, 2H), 3.13 (t, *J* = 8.4Hz, 1H), 2.20 (s, 3H), 2.11-2.02 (m, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 136.9, 131.6, 130.3, 129.3, 128.8, 128.41, 128.39, 127.9, 123.4, 33.1, 21.0, 20.9, 18.2.

FTIR (neat, cm<sup>-1</sup>): 3028, 2922, 2864, 2228, 1602, 1518, 1449, 1029, 970, 821, 698, 507.

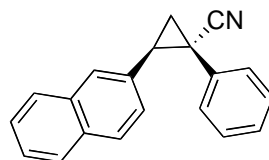
GC-MS (*m/z*): 233.

HRMS (EI<sup>+</sup>, *m/z*): 233.1193, calcd for C<sub>17</sub>H<sub>15</sub>N 233.1199.

mp (°C) 80-82.

[α]<sub>D</sub><sup>25</sup> = +74.6 (*c* = 0.84, CHCl<sub>3</sub>). [ee 83%]

ee 83% determined by chiral HPLC [OD, 0.8 mL/min, 0.7% isopropanol in hexanes, *t<sub>R</sub>* = 19.8 min (major) and 24.7 min (minor), UV 230nm].



**(1S, 2R)- 2-(Naphthalen-2-yl)-1-phenylcyclopropanecarbonitrile (6c):** Cyclopropane **6c** was obtained as a white solid, purified by 15:1 to 9:1 hexanes to diethyl ether using SiO<sub>2</sub> gel.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.70-7.64 (m, 2H), 7.56 (d, *J* = 8.0Hz, 1H), 7.43-7.37 (m, 3H), 7.16-7.09 (m, 5H), 6.96 (dd, *J* = 8.8Hz, *J* = 2.0Hz, 1H), 3.32 (t, *J* = 8.4Hz, 1H), 2.24-2.18 (m, 2H).

<sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>): δ 132.9, 132.4, 131.3, 131.1, 129.2, 128.5, 128.0, 127.7, 127.6, 127.54, 127.53, 126.3, 126.2, 125.9, 123.2, 33.5, 21.2, 18.4.

FTIR (neat, cm<sup>-1</sup>): 3058, 2925, 2228, 1600, 1500, 1448, 980, 859, 817, 749, 698.

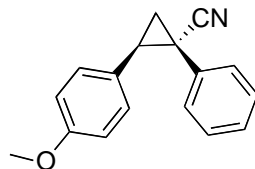
GC-MS (*m/z*): 269.

HRMS (EI<sup>+</sup>, *m/z*): 269.1201, calcd for C<sub>20</sub>H<sub>15</sub>N 269.1199.

mp ( $^{\circ}\text{C}$ ) 121-123.

$[\alpha]_{\text{D}}^{25} = +140.3$  ( $c = 1.14$ ,  $\text{CHCl}_3$ ). [ee 84%]

ee 84% determined by chiral HPLC [OD, 1.0 mL/min, 1.0% isopropanol in hexanes,  $t_{\text{R}} = 27.2$  min (major) and 33.5 min (minor), UV 230nm].



**(1S,2R)- 2-(4-Methoxyphenyl)-1-phenylcyclopropanecarbonitrile (6d):** Cyclopropane **6d** was obtained as a white solid, purified by 15:1 to 9:1 hexanes to diethyl ether using  $\text{SiO}_2$  gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.17-7.09 (m, 5H), 6.82 (d,  $J = 8.4\text{Hz}$ , 2H), 6.64 (d,  $J = 8.8\text{Hz}$ , 2H), 3.70 (s, 3H), 3.12 (t,  $J = 9.2\text{Hz}$ , 1H), 2.09 (dd,  $J = 9.6\text{Hz}$ ,  $J = 6.4\text{Hz}$ , 1H), 2.02 (dd,  $J = 7.6\text{Hz}$ ,  $J = 6.4\text{Hz}$ , 1H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  158.7, 131.6, 129.7, 129.2, 128.4, 127.8, 125.3, 123.4, 113.5, 55.1, 32.9, 20.8, 18.3.

FTIR (neat,  $\text{cm}^{-1}$ ): 3029, 2837, 2228, 1612, 1516, 1450, 1250, 1180, 1033, 833, 699.

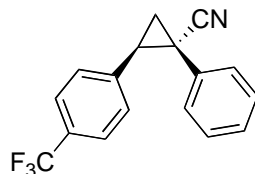
GC-MS ( $m/z$ ): 249.

HRMS ( $\text{EI}^+$ ,  $m/z$ ): 249.1148, calcd for  $\text{C}_{17}\text{H}_{15}\text{ON}$  249.1148.

mp ( $^{\circ}\text{C}$ ) 91-93.

$[\alpha]_{\text{D}}^{25} = +60.6$  ( $c = 0.51$ ,  $\text{CHCl}_3$ ). [ee 78%]

ee 78% determined by chiral HPLC [OD, 1.0 mL/min, 3.0 % isopropanol in hexanes,  $t_{\text{R}} = 13.1$  min (major) and 18.4 min (minor), UV 230nm].



**(1S,2R)- 1-Phenyl-2-(4-(trifluoromethyl)phenyl)cyclopropanecarbonitrile (6e):** Cyclopropane **6e** was obtained as an off-white solid, purified by 15:1 to 9:1 hexanes to diethyl ether using  $\text{SiO}_2$  gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.36 (d,  $J = 8.4\text{Hz}$ , 2H), 7.20-7.09 (m, 5H), 6.98 (d,  $J = 8.4\text{Hz}$ , 2H), 3.19 (t,  $J = 8.0\text{Hz}$ , 1H), 2.21-2.10 (m, 2H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  137.7, 130.8, 129.7, 129.3, 128.8, 128.7, 128.4, 125.0 (q,  $J = 3.5$  Hz), 123.9 (q,  $J = 271.9\text{Hz}$ ), 122.7, 32.6, 21.6, 18.3.

FTIR (neat,  $\text{cm}^{-1}$ ): 3031, 2924, 2231, 1621, 1326, 1167, 1123, 1070, 844, 699.

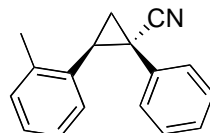
GC-MS (m/z): 287.

HRMS ( $\text{EI}^+$ , m/z): 287.0919, calcd for  $\text{C}_{17}\text{H}_{12}\text{NF}_3$  287.0916.

mp ( $^\circ\text{C}$ ) 69-71.

$[\alpha]_{\text{D}}^{25} = +55.7$  ( $c = 0.97$ ,  $\text{CHCl}_3$ ). [ee 90%]

ee 90% determined by chiral HPLC [OD, 1.0 mL/min, 0.8% isopropanol in hexanes,  $t_{\text{R}} = 18.6$  min (major) and 27.2 min (minor), UV 230nm].



**(1S,2R)- 1-Phenyl-2-*o*-tolylcyclopropanecarbonitrile (6f):** Cyclopropane **6f** was obtained as a white solid, purified by 15:1 to 9:1 hexanes to diethyl ether using  $\text{SiO}_2$  gel.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.11-6.99 (m, 8H), 6.92 (d,  $J = 7.5\text{Hz}$ , 1H), 3.16 (t,  $J = 9.0\text{Hz}$ , 1H), 2.27 (s, 3H), 2.21-2.14 (m, 2H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  138.7, 131.5, 131.4, 129.9, 128.0, 127.9, 127.7, 127.4, 127.2, 125.5, 123.1, 33.8, 20.5, 19.7, 18.5.

FTIR (neat,  $\text{cm}^{-1}$ ): 3027, 2230, 1601, 1495, 1031, 769, 696.

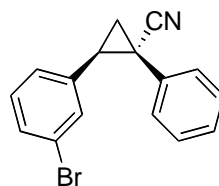
GC-MS (m/z): 233.

HRMS ( $\text{EI}^+$ , m/z): 233.1200, calcd for  $\text{C}_{17}\text{H}_{15}\text{N}$  233.1199.

mp ( $^\circ\text{C}$ ) 88-89.

$[\alpha]_{\text{D}}^{25} = +47.1$  ( $c = 0.87$ ,  $\text{CHCl}_3$ ). [ee 83%]

ee 83% determined by chiral HPLC [OD, 1.0 mL/min, 1.0 % isopropanol in hexanes,  $t_{\text{R}} = 11.7$  min (major) and 13.4 min (minor), UV 230nm].



**(1S,2R)- 2-(3-Bromophenyl)-1-phenylcyclopropanecarbonitrile (6g):** Cyclopropane **6g** was obtained as a white solid, purified by 15:1 to 9:1 hexanes to diethyl ether using SiO<sub>2</sub> gel.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.24-7.19 (m, 4H), 7.12-7.10 (m, 2H), 7.06 (s, 1H), 6.96 (t, *J* = 8.0Hz, 1H), 6.78 (d, *J* = 7.5Hz, 1H), 3.12 (t, *J* = 8.5Hz, 1H), 2.13 (dd, *J* = 6.0Hz, *J* = 9.0Hz, 1H), 2.07 (t, *J* = 8.0Hz, 1H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 135.9, 131.7, 130.9, 130.4, 129.5, 129.2, 128.6, 128.3, 127.2, 122.8, 122.1, 32.5, 21.3, 18.1.

FTIR (neat, cm<sup>-1</sup>): 3061, 2229, 1598, 1449, 1075, 778, 697.

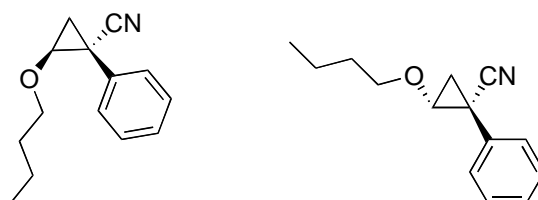
GC-MS (*m/z*): 297.

HRMS (EI<sup>+</sup>, *m/z*): 297.0150, calcd for C<sub>16</sub>H<sub>12</sub>NBr 297.0148.

mp (°C) 134-135.

[α]<sub>D</sub><sup>25</sup> = +78.9 (*c* = 1.21, CHCl<sub>3</sub>). [ee 90%]

ee 90% determined by chiral HPLC [OD, 1.0 mL/min, 0.4 % isopropanol in hexanes, *t<sub>R</sub>* = 53.8 min (major) and 66.5 min (minor), UV 230nm].



**Mixture of (1S,2S)- 2-butoxy-1-phenylcyclopropanecarbonitrile and (1S,2R)- 2-butoxy-1-phenylcyclopropanecarbonitrile (6h (major) and 6h (minor)):** Cyclopropanes **6h (major)** and **6h (minor)** were inseparable and obtained as a thick sap, purified by 15:1 to 5:1 hexanes to diethyl ether using SiO<sub>2</sub> gel.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.42 (d, *J* = 7.5Hz, 2H), 7.37-7.34 (m, 4H), 7.31-7.23 (m, 4H), 3.94 (dd, *J* = 7.0Hz, *J* = 5.0Hz, 1H), 3.85-3.81 (m, 1H), 3.69-3.65 (m, 1H), 3.58 (dd, *J* = 5.0Hz, *J* = 6.5Hz, 1H), 3.43-3.38 (m, 1H), 3.09-3.05 (m, 1H), 1.98 (dd, *J* = 5.0Hz, *J* = 7.5Hz, 1H), 1.90-1.82 (m, 2H), 1.75 (t, *J* = 6.5Hz, 1H), 1.70-1.64 (m, 2H), 1.44 (sextet, *J*

= 7.5Hz, 2H), 1.29-1.23 (m, 2H), 1.13-0.98 (m, 2H), 0.95 (t,  $J = 7.0\text{Hz}$ , 3H), 0.71 (t,  $J = 7.5\text{Hz}$ , 3H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.8, 130.6, 129.0, 128.3, 127.6, 127.4, 127.3, 125.5, 121.8, 119.6, 71.7, 71.0, 66.1, 65.1, 31.5, 31.1, 23.6, 21.3, 20.6, 19.9, 19.2, 18.9, 13.8, 13.6.

FTIR (neat,  $\text{cm}^{-1}$ ): 2959, 2231, 1602, 1354, 1187, 1083, 696.

GC-MS ( $m/z$ ): 215.

HRMS ( $\text{EI}^+$ ,  $m/z$ ): 215.1301, calcd for  $\text{C}_{14}\text{H}_{17}\text{ON}$  215.1305.

ee 80% (major diastereomer) determined by HPLC [OJ, 0.7 mL/min, 0.4 % isopropanol in hexanes,  $t_{\text{R}}=16.5$  min (major) and 19.5 min (minor), UV 230nm]

ee 79% (minor diastereomer) determined by HPLC [OJ, 0.7 mL/min, 0.4 % isopropanol in hexanes,  $t_{\text{R}}=24.2$  min (major) and 27.6 min (minor), UV 230nm]



**(1S,2S)-2-Cyano-2-phenylcyclopropyl ethanoate and (1R,2S)-2-Cyano-2-phenylcyclopropyl ethanoate (6i (minor) and 6i (major))**: Cyclopropanes **6i (minor)** and **6i (major)** were obtained as a colorless oil, purified by 5:1 to 3:1 hexanes to diethyl ether using  $\text{SiO}_2$  gel.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.39-7.27 (m, 5H), 7.39-7.32 (m, 5H), 4.73 (t,  $J = 4.8\text{Hz}$ , 1H), 4.39 (dd,  $J = 5.0\text{Hz}$ ,  $J = 7.0\text{Hz}$ , 1H), 3.19 (s, 3H), 2.01 (dd,  $J = 5.0\text{Hz}$ ,  $J = 7.0\text{Hz}$ , 1H), 1.97 (d,  $J = 6.5\text{Hz}$ , 2H), 1.85 (t,  $J = 7.0\text{Hz}$ , 1H), 1.75 (s, 3H).

$^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.8, 170.1, 133.3, 129.8, 129.1, 128.73, 128.70, 128.5, 127.1, 120.6, 118.6, 57.7, 56.6, 29.7, 21.1, 20.6, 20.0, 19.7, 17.7.

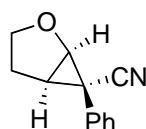
FTIR (neat,  $\text{cm}^{-1}$ ): 3062, 2920, 2850, 2236, 1756, 1364, 1211, 912, 697.

EI-MS ( $m/z$ ): 201.

HRMS ( $\text{EI}^+$ ,  $m/z$ ): 201.0789, calcd for  $\text{C}_{14}\text{H}_{17}\text{ON}$  201.0789.

92% ee (major diastereomer) determined by chiral HPLC [OJ, 0.8 mL/min, 10% isopropanol in hexanes,  $t_{\text{R}}= 24.4\text{min}$  (major) and 20.1min (minor), UV 230nm].

74% ee (minor diastereomer) determined by chiral HPLC [OD, 0.7 mL/min, 9% isopropanol in hexanes,  $t_{\text{R}}= 11.4\text{min}$  (major) and 13.2min (minor), UV 230nm].



**(1R,5R,6R)-6-Phenyl-2-oxabicyclo[3.1.0]hexane-6-carbonitrile (7):** Cyclopropane **7** was obtained as a white solid, purified by 1:1 hexanes to diethyl ether using SiO<sub>2</sub> gel.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.45-7.36 (m, 5H), 4.65 (d, *J* = 5.5Hz, 1H), 3.85-3.80 (m, 1H), 2.61 (t, *J* = 6.0Hz, 1H), 2.51 (q, *J* = 8.5Hz, 1H), 2.32-2.24 (m, 1H), 1.93-1.88 (m, 1H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 130.8, 129.2, 128.9, 120.5, 70.5, 67.7, 31.5, 25.7, 22.4.

FTIR (neat, cm<sup>-1</sup>): 3060, 2951, 2904, 2223, 1447, 1375, 1119, 1030, 938, 702.

EI-MS (*m/z*): 185.

HRMS (EI<sup>+</sup>, *m/z*): 185.0834, calcd for C<sub>12</sub>H<sub>11</sub>ON 185.0835.

mp (°C) 82-83.

[α]<sub>D</sub><sup>25</sup> = -6.8 (*c* = 0.13, CHCl<sub>3</sub>). [ee = 12%]

ee 12% (major diastereomer) determined by HPLC [OJ, 0.7 mL/min, 1.0% isopropanol in hexanes, *t<sub>R</sub>* = 48.8min (major) and 53.5min (minor), UV 230nm].



## X-ray Analysis: Experimental Details

Crystalline material of **6g** suitable for X-ray analysis was grown as follows: In a 25mL round bottom 350 mg of **6g** was dissolved in boiling absolute ethanol (~8 mL). Upon cooling to room temperature crystalline material of **6g** suitable for X-ray analysis were obtained. The crystalline material was found to have ee >98% by chiral HPLC.

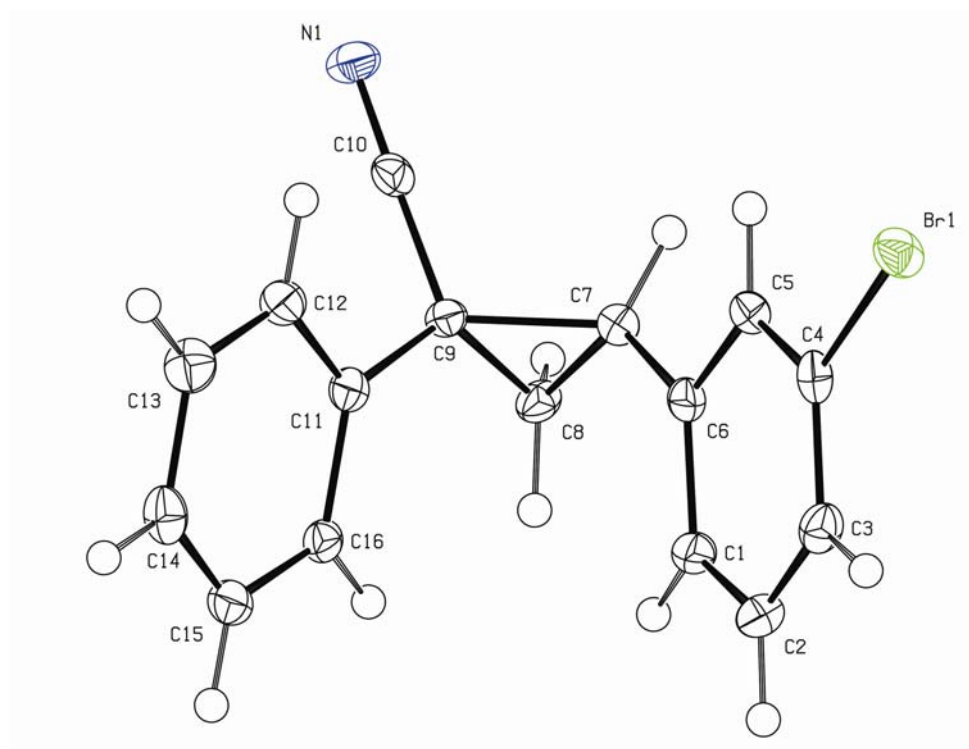


Fig. S1. ORTEP plot and label representation of cyclopropane **6g**. Displacement ellipsoids are drawn at the 50% probability level.<sup>4</sup>

<sup>4</sup> The X-ray crystallographic data has been submitted to the Cambridge Structure Database: M. Pitak, and P. Coppens, *Private Communication*, 2007, CCDC 654356.