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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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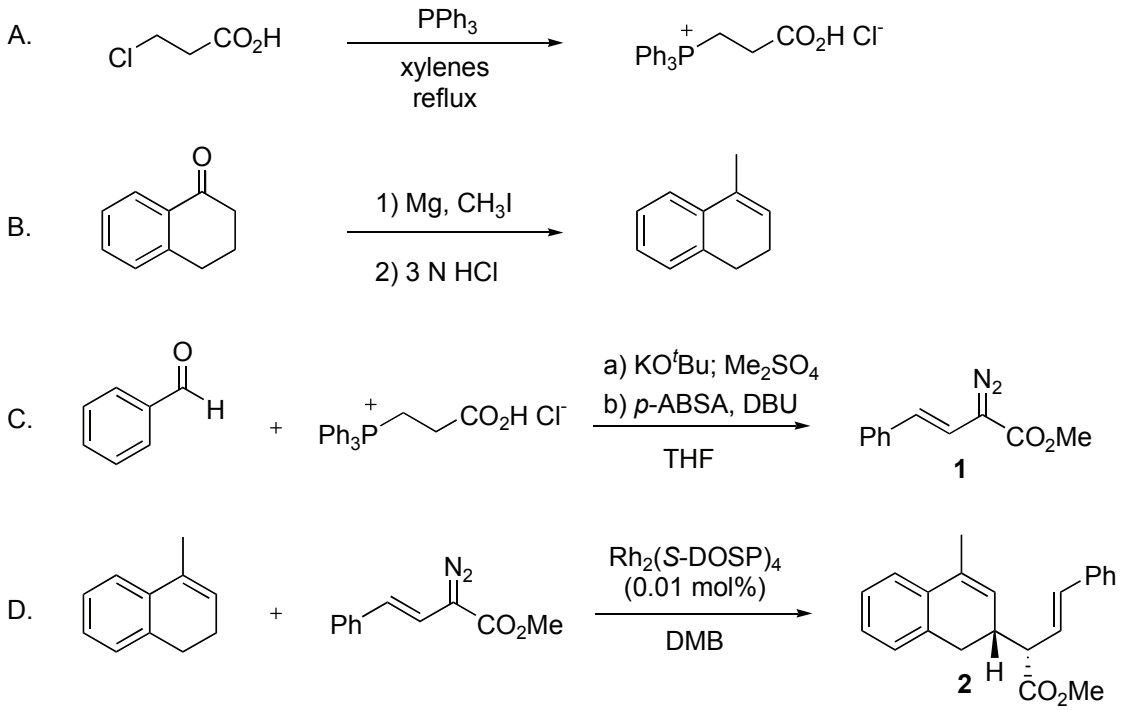
ONE-FLASK SYNTHESIS OF METHYL ARYLVINYLDIAZOACETATES AND THEIR APPLICATION IN ENANTIOSELECTIVE C–H FUNCTIONALIZATION: SYNTHESIS OF (*E*)-METHYL 2-DIAZO-4-PHENYLBUT-3-ENOATE AND (*S*,*E*)-METHYL 2-((*R*)-4-METHYL-1,2-DIHYDRONAPHTHALEN-2-YL)-4-PHENYLBUT-3-ENOATE



Submitted by James R. Manning and Huw M. L. Davies.[1]
Checked by Scott E. Denmark and William R. Collins.

1. Procedure

A. 2-Carboxyethyltriphenylphosphonium chloride. 3-Chloropropionic acid (16.3 g, 150 mmol) (Note 1) and triphenylphosphine (43.3 g, 165 mmol, 1.1 equiv) (Note 2) are added to a 250-mL, round-bottomed flask equipped with a magnetic stir bar. Xylenes (75 mL) (Note 3) are added and a water-cooled condenser is attached to the flask. Vigorous stirring is commenced and the solution is heated to reflux in an oil bath for 3 h during which time two layers form. The flask is then removed from the oil bath and the flask is fitted with a thermometer. When the solution has cooled to 60–70 °C, the thermometer is removed and acetonitrile (50 mL) (Note 4) is slowly added with vigorous stirring and scraping using a metal spatula to prevent the

product from sticking to the sides of the flask (Note 5). The product, which is eventually converted to a white solid, is collected by vacuum filtration in a Büchner funnel. The product is washed with diethyl ether (300 mL) (Note 6) and then dried under vacuum (0.05 mmHg) for 2 h to afford 46.6–46.7g (84%) of pure 2-carboxyethyltriphenylphosphonium chloride as a white solid (Note 7).

B. 1-Methyl-3,4-dihydronaphthalene. A 500-mL, 3-necked round-bottomed flask equipped with a stir bar is fitted with an argon inlet adaptor, a 100-mL pressure-equalized addition funnel and a reflux condenser. The tops of the addition funnel and reflux condenser are sealed with septa, the apparatus is flame dried under vacuum (0.05 mmHg) and then is backfilled with argon. Magnesium turnings (3.65 g, 150 mmol, 1.50 equiv) (Note 8) are then added and the flask is evacuated and filled with argon twice. Dry diethyl ether (100 mL) (Note 9) is added through the condenser via cannula. Iodomethane (9.98 mL, 22.7 g, 160 mmol, 1.60 equiv) (Note 10) is then added by syringe to the addition funnel. Stirring is commenced and the iodomethane is added dropwise to the magnesium turnings at a rate sufficient to maintain a gentle reflux (13–17 min is required to complete the addition). The solution is then stirred for another 20 min after the addition is complete. A solution of α-tetralone (14.6 g, 100 mmol) (Note 11) in dry diethyl ether (10 mL) is transferred via syringe from a flame-dried 100-mL round bottom flask to the addition funnel and then added dropwise to the methyl magnesium iodide solution at a rate sufficient to maintain a gentle reflux (12–16 min is required for the addition). The solution is stirred for another 15 min after completion of the addition. The rubber septa are then removed from the tops of both the condenser and the addition funnel. An aqueous solution of 3 N HCl (60 mL) is placed in the addition funnel and then is added dropwise to the solution over 30 min. The mixture is then vigorously stirred for 1 h at room temperature, after which time the mixture is poured into a 250-mL separatory funnel and the layers are separated. The aqueous layer is extracted with diethyl ether (3 x 30 mL). The combined ether extracts are washed with brine (50 mL), dried over anhydrous $MgSO_4$, vacuum filtered through a plug of silica gel (24 g) in a Büchner funnel and then concentrated by rotary evaporation at room temperature. The residue is purified by flash column chromatography on 130 g of silica gel (Note 12) eluting with pentane (450 mL). The fractions containing product are collected and concentrated by rotary evaporation (11 mmHg, room

temperature) to afford 13.1–13.2 g (91–92%) of pure 1-methyl-3,4-dihydronaphthalene as a clear oil (Notes 13, 14).

C. (E)-Methyl 2-diazo-4-phenylbut-3-enoate. 2-Carboxyethyl-triphenylphosphonium chloride (26.7 g, 72.0 mmol, 1.20 equiv) is added to a flame-dried, 2-necked 500-mL, round-bottomed flask equipped with a magnetic stir bar and fitted with a rubber septum and an argon inlet adaptor. The flask is evacuated (0.05 mmHg) and filled with argon two times after which a positive argon pressure is maintained on the flask. Benzaldehyde (6.07 mL, 6.37 g, 60.0 mmol) (Note 15) and THF (130 mL) (Note 16) are then added by syringe and the flask is externally cooled to 0 °C in an ice-water bath and vigorous stirring is begun. A solution of potassium *tert*-butoxide (16.8 g, 150 mmol, 2.5 equiv) in THF (80 mL) under an argon atmosphere and at 0 °C is then added *via* cannula under positive argon pressure over 30 min (Notes 16, 17). After the addition is complete, the solution is stirred at 0 °C for 30 min, then the ice-water bath is removed and stirring is continued for another 20 min. Dimethyl sulfate (11.4 mL, 15.1 g, 120 mmol, 2.0 equiv) (Note 18) is then added rapidly by syringe and stirring is continued at ambient temperature for 2.5 h. The septum is then briefly removed from the flask and *para*-acetamidobenzenesulfonyl azide (18.7 g, 78.0 mmol, 1.30 equiv) (Note 19) is added in one portion. The septum is replaced and the flask, under a positive argon pressure, is externally cooled to 0 °C in an ice-water bath. DBU (11.7 mL, 11.9 g, 78.0 mmol) (Note 20) is then added rapidly by syringe and the solution quickly becomes red. Stirring is continued at 0 °C for 4 h and then the solution is allowed to warm to room temperature and then is transferred to a 1-L, single-necked, round-bottomed flask and the solution is concentrated by rotary evaporation (27 mmHg, ambient temperature) (Note 21). The residue is treated with saturated aqueous ammonium chloride solution (150 mL) and diethyl ether (400 mL) and the mixture is poured into a 1-L separatory funnel and vigorously shaken. The aqueous layer is drained and the organic layer is washed with saturated ammonium chloride solution (150 mL) and then is dried over anhydrous $MgSO_4$ (5 g) (Note 22). The solvent is removed by rotary evaporation (11 mmHg, room temperature) to give a dark-red oil. The oil is then adsorbed onto 50 g of silica gel, which is then placed at the top of a packed column of silica gel (350 g) (Note 23). The column is eluted with pentanes/diethyl ether, 12:1. The red fractions containing the product are collected and concentrated by rotary evaporation at room temperature to afford 9.3–9.7 g (77–80%) of **1** as a red solid (Note 24).

D. (*S,E*)-*Methyl 2-((R)-4-methyl-1,2-dihydronaphthalen-2-yl)-4-phenylbut-3-enoate.* 1-Methyl-3,4-dihydronaphthalene (5.34 g, 37.0 mmol) and Rh_2(*S*-DOSP)$_4$ (7.0 mg, 0.0037 mmol, 0.0001 equiv) (Note 25) are added to a flame-dried, 250-mL 2-necked, round-bottomed flask equipped with a magnetic stir bar and fitted with an argon inlet adaptor and a rubber septum. The flask is evacuated (0.05 mmHg) and purged with argon twice and then maintained under a positive argon pressure. 2,2-Dimethylbutane (40 mL) (Note 26) is added by syringe and vigorous stirring is begun. A solution of (*E*)-methyl 2-diazo-4-phenylbut-3-enoate **1** (8.23 g, 40.7 mmol, 1.10 equiv) (Note 27) in 2,2-dimethylbutane (60 mL) is added by syringe pump over 4 h (Note 28). The solution is stirred for an additional 10 h and the solvent is then removed by rotary evaporation (11 mmHg, room temperature) to give a light-yellow solid. Absolute ethanol (20 mL) is added to the crude material and a reflux condenser is attached to the flask. The solution is heated to reflux to dissolve the material and then allowed to cool to room temperature, whereupon the product crystallizes as an off-white solid. The solution is then cooled to 0 °C for 2 h and the product is collected by vacuum filtration on a Büchner funnel to give 8.0–8.3 g (68–70%) of pure **2** as an off-white solid (Note 29).

2. Notes

1. 3-Chloropropionic acid was purchased from Acros Organics and used as received.
2. Triphenylphosphine was purchased from Acros Organics and used as received.
3. Xylenes were purchased from Mallinckrodt Inc. and used as received.
4. Acetonitrile was purchased from J. T. Baker and used as received.
5. Scraping the precipitated material was crucial to induce solidification of the product, which initially separated out of the xylene solution as a taffy-like material.
6. Washing should be continued with diethyl ether until the wash solvent no longer appears white after filtration.
7. The product displayed the following properties: mp 201–204 °C (sealed tube); IR (neat): cm^{-1} 2900, 1742, 1421, 1586, 1489, 1439, 1421, 1388, 1352, 1220, 1165, 1116, 1037, 996, 950, 910, 859, 816, 752, 698, 613;

^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.09–3.15 (m, 2 H), 3.69–3.75 (m, 2 H), 7.69–7.84 (m, 15 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.1, 28.1, 117.2, 130.4, 133.4, 171.3, 135.2; LRMS EI (relative intensity) *m/z*: 369 ($[M]^+$, 6), 317 (5), 262 (100), 183 (25), 152 (4); Anal. Calcd for $C_{21}H_{20}ClO_2P$: C, 68.02; H, 5.44. Found: C, 68.03; H, 5.48. The spectroscopic data were consistent with previously reported literature values.[2a,b] The procedure described herein is a modified version of a literature procedure.[2b]

8. Magnesium turnings were purchased from Fisher Scientific and used as received.

9. Diethyl ether was purchased from EMD Chemicals Inc., dried over 4Å molecular sieves overnight and further dried by pressure filtration through activated alumina.

10. Iodomethane (99%) was purchased from Aldrich Chemical Company, Inc. and used as received. It is classified as a carcinogen and should be handled with care

11. α-Tetralone was purchased from Aldrich Chemical Company, Inc. (98%) and used as received.

12. Silica gel was purchased from Silicycle (40-63 μm particle size, 60 Å pore diameter) and loaded as a slurry onto a 30-mm diameter column. Fractions were collected (19 mL) and elution monitored by TLC (silica gel, R_f 0.51, pentane).

13. The submitters occasionally found that the product was contaminated with the isomeric 1-methylene-1,2,3,4-tetrahydronaphthalene in a 25:1 ratio on some of the trials. This impurity was inseparable by chromatography but was converted quantitatively to the desired product by refluxing the mixture in toluene with 1 mol % toluenesulfonic acid monohydrate for 1 h.

14. The product displayed the following properties: R_f 0.51 (pentanes); IR (neat): cm^{-1} 3097, 3060, 2933, 2883, 2830, 2856, 1487, 1450, 1438, 1427, 1378, 1239, 1069, 1039, 1020, 936, 886, 868, 812, 791, 756, 731, 704, 633; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.09 (s, 3 H), 2.27–2.31 (m, 2 H), 2.79 (t, *J*=8.5 Hz, 2 H), 5.88 (m, 1 H), 7.17–7.22 (m, 2 H), 7.22–7.29 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 23.4, 28.6, 122.9, 125.6, 126.5, 126.9, 127.6, 132.4, 136.1, 136.5; LRMS EI (relative intensity) *m/z*: 144 ($[M]^+$, 100), 129 (47), 115 (10), 102 (4), 89 (5), 77 (3), 63 (5); Anal. Calcd for $C_{11}H_{12}$: C, 91.61; H, 8.39. Found: C, 91.57; H, 8.22. The spectroscopic data were consistent with previously reported literature values.[3] The procedure described herein is a modified version of a literature procedure.[3]

15. Benzaldehyde (redistilled, 99.5+%) was purchased from Aldrich Chemical Company, Inc. and used as received.

16. THF was purchased from J. T. Baker Chemical Co., dried over 4 Å molecular sieves overnight and further dried by pressure filtration through activated alumina.

17. Potassium *tert*-butoxide (98+%) was purchased from Acros Organics and used as received. The solution in THF was cooled externally to 0 °C in an ice-water bath before and during addition.

18. Dimethyl sulfate was purchased from Acros Organics and used as received. It is classified as a carcinogen and should be handled with care.

19. *p*-Acetamidobenzenesulfonyl azide (*p*-ABSA) is commercially available (Aldrich Chemical Company, Inc.), but was prepared by the submitters using the published procedure, See *Org. Synth., Coll. Vol. IX* **1998**, 422. Although the compound has not exhibited shock sensitivity,[4] *all azide compounds should be handled with care*.

20. DBU was purchased from Acros Organics and used as received.

21. The reaction mixture was concentrated on a rotary evaporator in a fume hood because of the excess dimethyl sulfate that was collected in the receiver.

22. Anhydrous $MgSO_4$ was purchased from Fisher Scientific Company.

23. Silica gel was purchased from Silicycle (40–63 μm particle size, 60 Å pore diameter) and loaded as a slurry onto a 60-mm diameter column.

24. The product displayed the following properties: R_f 0.35 (9:1 pentane/ether); IR (neat): cm^{-1} 2960, 2168, 2088(C=N_2), 1706, 1626, 1492, 1449, 1438, 1405, 1364, 1318, 1286, 1243, 1194, 1113, 1010, 950, 752, 734, 692; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.86 (s, 3 H), 6.20 (d, *J* =16.0 Hz, 1 H), 6.49 (d, *J*= 16.0 Hz, 1 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 7.30–7.37 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 52.05, 111.0, 122.8, 125.6, 126.8, 128.4, 136.5, 165.0; LRMS EI (relative intensity) *m/z*: 202.1 ($[M]^+$, 38), 170.0 (10), 159 (4), 142 (12), 129 (16)); Anal. Calcd for $C_{11}H_{10}N_2O_2$ C, 65.34; H, 4.98; N, 13.85, Found: C, 65.40; H, 4.94; N, 13.70 The procedure described herein is a modified version of a literature procedure.[5] The product should be stored at 0 °C and immediately purified before use if stored for more than ~2 days as it will slowly undergo an electrocyclization reaction to form a pyrazole. The pyrazole is observed as a white crystalline solid. *All diazo compounds should be handled carefully,* although in this case, the only thermal decomposition pathway exhibited by this compound in the absence of

catalyst is electrocyclization to the pyrazole. The compound should not be stored in solution as this accelerates the decomposition reaction.

25. Rh_2(*S*-DOSP)$_4$ is commercially available from Strem Chemicals, Inc. and Aldrich Chemical Company, Inc. and is air stable. Alternatively, it can be readily made by the published procedure.[6]

26. 2,2-Dimethylbutane (DMB) was purchased from Lancaster Synthesis and distilled from sodium under argon prior to use.

27. (*E*)-Methyl 2-diazo-4-phenyl-3-butenoate **1** was freshly purified when used. The checkers found that 500 μL of diethyl ether was needed to wet the solid before it was diluted with DMB. If the diethyl ether was not used, the starting material was not completely soluble in the DMB.

28. The checkers found that carrying out the syringe pump addition with a 50-mL syringe led to clogging from formation of the insoluble pyrazole. The best results were obtained by carrying out the addition in six portions with a 10-mL syringe with a 16-gauge needle (40 min per addition for the total of a 4-h addition period).

29. The product was obtained in 87–92% yield when purified by silica gel column chromatography (See Table 2), but contained a slight greenish tinge. The product displayed the following properties: mp 77–79 °C (sealed tube), R_f 0.35 (10:1 pentane/ether); IR (KBr): cm^{-1} 2946, 1956, 1886, 1735, 1638, 1487, 1450, 1427, 1380, 1331, 1298, 1264, 1215, 1151, 1098, 1024, 993, 972, 944, 902, 842, 807, 761, 723, 659; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.07 (s, 3 H), 2.72 (m, 1 H), 2.84–2.88 (m, 2 H), 3.11 (t, *J*=9.5 Hz, 1 H), 3.69 (s, 3 H), 5.73 (d, *J*=3.5 Hz, 1 H), 6.14 (dd, *J*=16.0, 9.5 Hz, 1 H), 6.42 (d, *J*=16.0 Hz, 1 H), 7.08 (d, *J*= 7.0 Hz, 1 H), 7.15 (td, *J*= 7.0, 2.0 Hz, 1 H), 7.23–7.24 (m, 4 H), 7.30–7.36 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.4 (CH_3), 31.7, 36.1, 51.9, 53.2, 123.0, 126.0, 126.2, 126.4, 126.6, 127.2, 127.7, 127.8, 128.5, 134.4, 135.3, 136.6, 173.6; LRMS ESI (relative intensity) *m/z*: 319.2 ($[M+H]^+$,7), 341.1 ($[M+Na]^+$, 0.4), 287 (3), 259.1 (3), 176 (100), 143 (94); HPLC analysis: >99.8:0.2 (unable to accurately integrate minor enantiomer) (Chiralcel OD-H, 2% *i*-PrOH in hexane, 0.8 mL/min, λ = 254 nm, t_R = 7.25 min , major; t_R = 7.99 min, minor); Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.99; H, 6.96. Found: C, 82.62; H, 6.94. $[\alpha]_D$ = –21.4 (c = 1.0, ethanol). The procedure described herein is a modified version of a literature procedure.[7]

Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

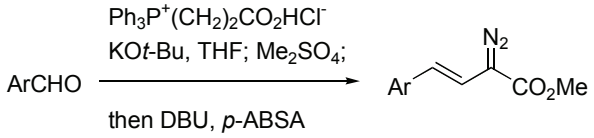
3. Discussion

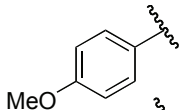
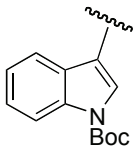
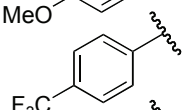
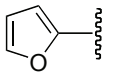
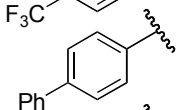
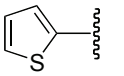
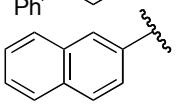
Dirhodium tetracarboxylate based catalysts efficiently decompose diazo compounds to generate reactive metal carbenoids that are capable of undergoing extraordinarily regio- and stereoselective reactions.[8] This is especially true when such catalysts are used in conjunction with diazo compounds that contain both electron-donating groups (EDG) and electron-withdrawing groups (EWG). Our work over the last decade in this area has shown that the prolinate based catalyst Rh_2(*S*-DOSP)$_4$ and its second generation relative, the bridged catalyst Rh_2(*S*-biTISP)$_2$ can routinely produce highly diastereo- and enantioselective intermolecular cyclopropanation reactions with the latter catalyst capable of achieving very high turnover numbers (92,000).[9]

While highly stereoselective cyclopropanation reactions have been known for some time, asymmetric intermolecular C–H activation reactions are a more recent development. Extensive work in this area in recent years has led to carbenoid surrogates for many classic organic transformations including the aldol addition,[10] the Mannich reaction,[11] and the Claisen rearrangement.[12] Rh_2(*S*-DOSP)$_4$ has been an exceptional catalyst for these transformations and has been found to perform best with diazo compounds substituted with both a methyl ester (EWG) and an aryl, heteroaryl, or vinyl group (EDG). C–H activation products are regularly formed as single diastereomers and with >90% ee. One of the more spectacular transformations discovered in recent years using this catalyst has been the combined C–H activation/Cope rearrangement reaction.[7,13] It occurs when a vinyl-substituted carbenoid undergoes a C–H activation of an allylic C–H bond that is interrupted by a Cope rearrangement. The product of this transformation will then normally undergo a retro-Cope rearrangement at room temperature or upon heating in toluene to give the thermodynamically more stable "formal" C–H activation product. This transformation is extremely efficient with dihydronaphthalenes as substrates and routinely produces products in high yields and with >98% ee. The process is

amenable to a variety of vinyldiazoacetates and substituted dihydronaphthalenes. The procedure described here can be used to synthesize many different vinyldiazoacetates starting from readily available aromatic aldehydes. Several examples of this are shown in Table 1,[5] performed on a 5-mmol scale.

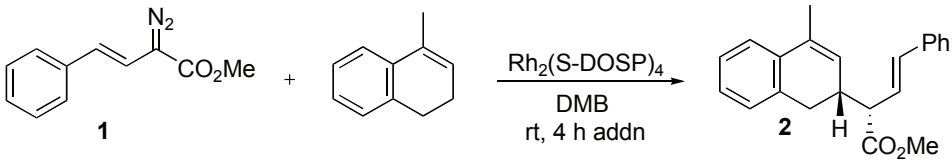
Table 1.



Ar	Yield (%)	Ar	Yield (%)
	65		49
	46		69
	49		62
	55		

The combined C–H activation/Cope rearrangement reaction has proven to be a very favorable transformation and catalyst loadings as low as 0.01 mol% can be used with no significant drop in yield or stereoselectivity (Table 2).

Table 2.



diazo (mmole)	substrate (mmole)	catalyst (mole %)	catalyst T.O.	yield[a] (%)	de (%)	ee (%)
1.20	1.00	0.10	920	92	>94	99.3
12.0	10.0	0.050	1740	87	>94	99.4
12.0	10.0	0.040	2300	92	>94	99.5
12.0	10.0	0.030	2967	89	>94	99.7
12.0	10.0	0.020	4550	91	>94	99.2
12.0	10.0	0.010	9100	91[b]	>94	99.5
12.0	10.0	0.0075	-	73[c]	>94	97.3

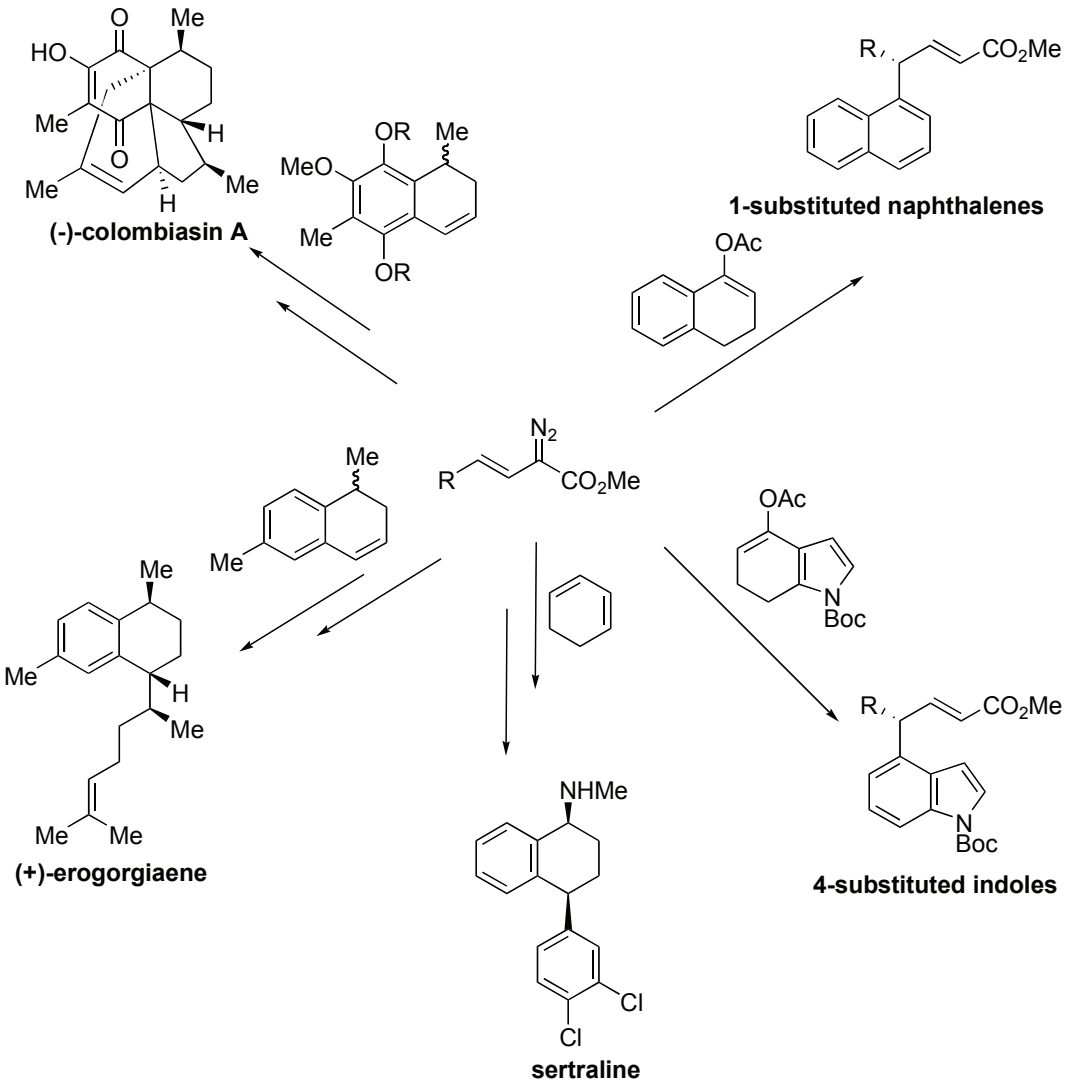
[a] isolated yield after flash column chromatography

[b] solution was green at the end of addition-TOF at least 2275 h^{-1}

[c] reaction incomplete-yield from crude ^1H NMR ratio of product:sm (2.7:1)

The procedure described here is readily performed on a large scale, as the amount of catalyst required is small compared to the product generated and the crude reaction mixture is easily recrystallized from ethanol to give the pure product, requiring no other purification steps. Although the sequence is illustrated with a methyl-substituted dihydronaphthalene, unsubstituted substrates and other substituents, including siloxy and acetoxy, can be used.[7] This methodology has been successfully used in a variety of applications, including total synthesis (Scheme 1).[7,13]

Scheme 1.



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2. (a) Denney, D. B.; Smith, L. C. *J. Org. Chem.* **1962**, *27*, 3404-3408. (b) Narayanan, K. S.; Berlin, K. D. *J. Org. Chem.* **1980**, *45*, 2240-2243.
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Appendix
Chemical Abstracts Nomenclature; (Registry Number)

3-Chloropropionic acid: Propanoic acid, 3-chloro-; (107-94-8)
Triphenylphosphine; (603-35-0)
2-Carboxyethyltriphenylphosphonium chloride; (36626-29-6)

Iodomethane; (74-88-4)
Magnesium (7439-95-4)
α-Tetralone: 1(2H)-Naphthalenone, 3,4-dihydro-; (529-34-0)
1-Methyl-3,4-dihydronaphthalene: Naphthalene, 1,2-dihydro-4-methyl-; (4373-13-1)
(*E*)-Methyl 2-diazo-4-phenylbut-3-enoate: (119987-21-2)
Benzaldehyde; (100-52-7)
Potassium *tert*-butoxide: 2-Propanol, 2-methyl-, potassium salt (1:1); (865-47-4)
Dimethyl sulfate: Sulfuric acid, dimethyl ester; (77-78-1)
p-Acetamidobenzenesulfonyl azide: Benzenesulfonyl azide, 4-(acetylamino)-; (2158-14-7)
DBU: Pyrimido[1,2-a]azepine, 2,3,4,6,7,8,9,10-octahydro-; (6674-22-2)
(*S,E*)-Methyl 2-((*R*)-4-methyl-1,2-dihydronaphthalen-2-yl)-4-phenylbut-3-enoate: 2-Naphthaleneacetic acid, 1,2-dihydro-4-methyl-α-[(1E)-2-phenylethenyl]-, methyl ester, (αS,2R)-; (76531-50-5)
Rh_2(*S*-DOSP)$_4$; (179162-34-6)

Huw M. L. Davies was born in Aberystwyth, Wales, UK. He received his B.Sc. from University College Cardiff, Wales and his Ph.D. from the University of East Anglia, England. After a post-doctoral position at Princeton University, he joined the faculty at Wake Forest University. In 1995 he moved to the University at Buffalo, the State University of New York, where he currently holds the position of UB Distinguished Professor and Larkin Professor of Organic Chemistry. His research program covers design of chiral catalysts, development of new synthetic methodology, total synthesis of biologically active natural products, and development of chiral therapeutic agents. A major current theme is catalytic asymmetric C–H functionalization by means of rhodium-carbenoid induced C–H insertion.

James R. Manning was born in 1979 in Swanton, Vermont. He received his B.S. degree in chemistry (2002) from the University of Vermont while performing undergraduate research in the laboratory of Professor Gregory K. Friestad. He is currently a doctoral student at the University at Buffalo, The State University of New York under the guidance of Professor Huw M. L. Davies. His research is focused on the exploration of rhodium-catalyzed intermolecular carbenoid reactions in the context of methodology development for the synthesis of pharmaceutically relevant compounds and natural product synthesis. Mr. Manning is the recipient of an NIH predoctoral fellowship.

William R. Collins' interest in organic chemistry began at the New Mexico Institute of Technology during an undergraduate project under Dr. Michael Heagy which involved the design and synthesis of boronic acid chemosensors for carbohydrate recognition. After a National Science Fellowship Undergraduate Research Experience (NSF REU) in 2001 at the University of New Mexico with Dr. Patrick Mariano studying photochemically induced macrocyclizations of phthalimides, he became more interested in synthesis and methodology. His current project focuses on expansion of the scope of the Lewis base catalyzed asymmetric variant of the Passerini reaction.