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Efficient one-pot synthesis of 1-arylcycloprop-2-ene-1-carboxamides

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Abstract

An expeditious and cost-efficient method for synthesis of 1-arylcycloprop-2-ene-1-carboxamides was developed. This one-pot protocol involving coupling of amines with acyl chlorides, generated upon treatment of cyclopropylcarboxylic acids with oxalyl chloride, is applicable for the preparation of sensitive products with a reactive, unsubstituted strained double bond.

Abstract

Introduction

Cycloprop-2-ene-1-carboxamides (**3**) have proven themselves as a more stable and versatile alternative to readily available but much more reactive cycloprop-2-ene-1-carboxylates (**1**). Being an efficient electron-withdrawing group, the carboxamide function stabilizes the reactive strained double bond; however, unlike esters, amides are much less sensitive to strong bases and are compatible with the conditions used for generation of cyclopropenyl anion (**4**) (path **a**, Scheme 1).¹ Carboxamide substituents can be used to control facial selectivity in addition reactions to cyclopropenes, as was demonstrated in the sterically-controlled palladium-catalyzed addition of H-P entities (path **b**)² and carboxamide-directed, base-assisted nucleophilic additions of alkoxides and azoles (path **c**).³ The amide functionality could also serve as an efficient electron-pulling entity to trigger “push-pull” ring-opening in the nucleophilic addition of amines to cyclopropenes (path **d**, Scheme 1).⁴

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The application of amides in bioorthogonal transformations for installation of the cyclopropene moiety into biological probes has also been shown recently.⁵

Our ongoing studies of reactivity of cyclopropylcarboxamides in transition metal-catalyzed reactions⁶ required access to a series of 1-arylcycloprop-2-ene-1-carboxamides (**3**, $R^1 = \text{Ar}$, $R^2 = \text{H}$) with a non-substituted double bond. However, the existing literature lacks methods expressly designed for synthesis of these substrates. This motivated us for the development of a practical approach to cyclopropenylcarboxamides **3** ($R^2 = \text{H}$) from 1,2-unsubstituted 1-arylcycloprop-2-ene-1-carboxylates (**1**, $R^2 = \text{H}$)⁷ that we report herein.

Results and Discussion

We have previously reported a convenient method for the installation of a cyclopropene moiety in the presence of a carboxamide group via a 1,2-elimination reaction of 2-bromocyclopropanes **10** (Scheme 2, eq. 1).^{1,8} However, this approach was limited to the preparation of cyclopropene-3-carboxamides **11** possessing a methyl group at C3. Another expedient method is the catalytic cyclopropenation of terminal alkynes **12** with a carbenoid species generated from α -diazoacetamides **13** (Scheme 2, eq. 2),⁹ with its asymmetric version allowing for single step preparation of enantiomerically enriched 1-substituted products (**3**, $R^2 = \text{Alk, Ar}$). Yet this method has not been used for synthesis of 1,2-unsubstituted analogs (**3**, $R^2 = \text{H}$) and is applicable to preparation of tertiary amides only, which must be installed very early in the synthesis.

We have recently developed a practical protocol, involving catalytic cyclopropenation of trimethylsilylacetylene **14** with α -diazoacetates **15**,⁷ followed by desilylation and hydrolysis to obtain 1,2-unsubstituted carboxylic acids **17**. We envisioned that acids **17** could be convenient precursors for amides **18**. Among the numerous methods used in peptide chemistry for the installation of an amide moiety, only a few have been probed for the preparation of sensitive cyclopropene-containing products. Thus, Fox used direct peptide coupling of 1-butyl-cyclopropene-3-carboxylic acid derivatives activated by HCTU.¹⁰ However, our attempts to adopt this protocol for synthesis of more sensitive, “non-substituted” amide **18aa** provided inconsistent results. Although acylation of amide proceeded cleanly, isolated yields were low due to significant loss of the product during chromatographic purification. An alternative synthetic route involving acylation of amines with perfluorophenyl- or 2,5-dioxopyrrolidin-1-yl cyclopropene-3-carboxylates reportedly provided moderate yields in submilligram scale peptide coupling of non-bulky derivatives of cyclopropene-3-carboxylic acid **17** ($R^1 = \text{H, Me}$).^{5,11} However, adaptation of this protocol for preparative scale synthesis of small compound libraries would be cost-prohibitive. Another foreseen problem of using perfluorophenyl trifluoroacetate or NCS as coupling agents is the formation of organic byproducts, which would complicate post-reaction work up. Accordingly, coupling reagents producing only water-soluble inorganic byproducts would be preferred. Among these we considered thionyl and oxalyl chlorides, both being low-boiling reagents that convert carboxylic acids into more reactive acyl chlorides with only gaseous by-products. Treatment of **17a** with SOCl_2 and diethylamine (**20a**) provided complex mixtures of products; however, the analogous reaction with oxalyl chloride carried out at room temperature in the presence of catalytic amounts of DMF proceeded slowly but

very cleanly affording crude acyl chloride **19a** ($R^1 = \text{Ph}$). The latter was used without isolation in the subsequent reaction with diethylamine (**20a**) to provide amide **18aa** as a sole product in 89% yield (Table 1, entry 1). These reaction conditions seemed to be optimal, since our attempts to accelerate the process by raising the reaction temperature led to notable deterioration of the yield, due to a side reaction involving nucleophilic attack of excess secondary amine across the double bond of cyclopropene.⁴

With the optimized conditions in hand we tested the scope and compatibility of this transformation. First, carboxylic acid **17a** was treated with oxalyl chloride and various secondary amines. Diallylamine (**20c**) and various benzyl-amines (**20d-g**) reacted uneventfully providing high yields of amides **18ac-ag** (entries 3-7). Expectedly, the reaction with sterically hindered diisopropylamine (**20b**) proceeded very sluggishly, affording amide **18ab** in somewhat lower yield (Table 1, entry 2). Attempts to install a more bulky and less nucleophilic diphenylamine moiety proved inefficient, as the initially formed amide **18ah** completely hydrolyzed upon aqueous work-up (entry 8). A series of cyclic secondary amines, such as pyrrolidine (**20i**), piperidine (**20j**), morpholine (**20k**), and *N*-ethylpiperazine (**20l**) were also probed, affording the corresponding amides **18ai-18al** in excellent yields (entries 9-12). Likewise, all primary amines tested (**20m-20p**), reacted smoothly to give the secondary amides **18am-18ap** (entries 13-16). In order to employ the carboxamide moiety as a directing group in transition metalcatalyzed and ion-templated, base-assisted addition reactions,³ we also required access to cyclopropene-3-carboxamides possessing an additional chelating group, to which end we performed reactions with 2-picolylamine (**20q**) and furfurylamine (**20r**) (entries 17-18). A binucleophilic 2-aminoethanol (**20s**) provided amide **18as** in moderate yield only (entry 19), which can potentially be attributed to a concurrent nucleophilic addition of the alkoxide to the cyclopropane double bond.³ Employment of aqueous ammonia (**20t**) gave rise to primary amide **18at** (entry 20). Acylation of *N,O*-dimethyl-hydroxylamine (**20u**) afforded the synthetically useful Weinreb amide **18au** (entry 21). Other 1-arylcycloprop-2-ene-1-carboxylic acids (**17b-d**) efficiently reacted with diethylamine (**20a**) to give 2-naphthyl- (**18b**), 2,4-difluorophenyl- (**18c**), and 2-chloro-4-fluorophenyl- (**18d**) cyclopropenylcarboxamides, respectively (entries 22-24).

Additional evidence of the excellent reaction scope was obtained by employing 1-arylcycloprop-2-ene-1-carboxylic acids substituted at C2 (**2a,b**) (Scheme 3), which afforded the corresponding carboxamides **18ca-18da** (Table 1, entries 22-24) and **3a,b** (Scheme 3) in excellent yields. Finally, we have also explored the possibility to carry out a two-fold peptide coupling using two equivalents of acid **17a** with 1,2-ethylenediamine. We were pleased to find that the bis-cyclopropene **21** was obtained as a sole product, albeit in moderate yield (Scheme 4).

Conclusions

We have developed a convenient and cost-effective method for synthesis of 1-arylcycloprop-2-ene-1-carboxamides through peptide coupling of the parent cycloprop-2-ene-1-carboxylic acids. Mild reaction conditions involving “traceless” generation of acyl chlorides with oxalyl chloride and subsequent same pot reaction with amines proved to be fully compatible with the sensitive 2,3-unsubstituted cyclopropene moiety, allowing for

facile preparation of a broad array of cyclopropene amides. Further investigations of their reactivity are currently underway in our laboratories.

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Experimental part

NMR spectra were recorded on a Bruker Avance DRX-500 with a dual carbon/proton cryoprobe (CPDUL). ^{13}C NMR spectra were registered with broadband decoupling. The (+) and (–) designations represent positive and negative intensities of signals in ^{13}C DEPT-135 experiments. IR spectra were recorded on a Shimadzu FT-IR 8400S instrument. HRMS was carried out on LCT Premier (Micromass Technologies) instrument; ESI TOF detection techniques were used. Glassware employed in moisture-free syntheses was flame-dried in vacuum prior to use. A combination of glove box and standard Schlenk technique was used to handle moisture sensitive materials. Column chromatography was carried out on silica gel (Sorbent Technologies, 40–63 μm). Pre-coated silica gel plates (Sorbent Technologies Silica XG 200 μm) were used for TLC analyses. Anhydrous dichloromethane was obtained by passing degassed commercially available HPLC-grade inhibitor-free solvent consecutively through two columns filled with activated alumina and stored over molecular sieves under nitrogen. Water was purified by dual stage deionization followed by dual stage reverse osmosis. 1-Phenylcycloprop-2-enecarboxylic (**17a**),¹² 1,2-diphenylcycloprop-2-enecarboxylic (**2a**),¹³ and 2-butyl-1-phenylcycloprop-2-enecarboxylic (**2b**)¹⁴ acids were obtained according to the published procedure and had physical and spectral properties identical to those, reported in literature. Synthesis of esters: methyl 1-(naphthalen-1-yl)-2-(trimethylsilyl)cycloprop-2-enecarboxylate, methyl 1-(2,4-difluorophenyl)-2-(trimethylsilyl)cycloprop-2-enecarboxylate, and methyl 1-(2-chloro-4-fluorophenyl)-2-(trimethylsilyl)cycloprop-2-enecarboxylate was detailed in our recent report.⁷ All other reagents and solvents were purchased from commercial vendors and used as received.

1-(Naphthalen-2-yl)cycloprop-2-ene-1-carboxylic acid (**17b**) (typical procedure A)

Solution of methyl 1-(naphthalen-2-yl)-2-(trimethylsilyl)cycloprop-2-ene-1-carboxylate (513 mg, 1.73 mmol, 1.00 equiv.) in a 1:1 mixture of methanol:THF (20 mL) was stirred at 0°C. A 1.5M aqueous solution of NaOH (15 mL, 22.5 mmol, 13.0 equiv.) was added dropwise and the mixture was stirred for 18 h. Organic solvents were then removed under vacuum and the remaining aqueous solution was added to dichloromethane (20 mL). The mixture was acidified to pH 2 with 1N aqueous HCl. Organic phase was separated, and the aqueous layer was extracted with dichloromethane (3 $\times$ 10 mL). The combined organic phases were washed with brine, dried with MgSO_4 , filtered, and concentrated. The obtained product is typically pure enough to be used in further amide coupling as is, however, if necessary, further purification could be achieved by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc. The titled compound was obtained as a colorless solid, mp 188–190 °C (dec), R_f 0.27, yield 332 mg (1.58 mmol, 91%). ^1H NMR (500 MHz,

CDCl₃): δ 8.11 – 8.04 (m, 1H), 7.88 – 7.82 (m, 1H), 7.78 – 7.75 (m, 1H), 7.57 – 7.46 (m, 2H), 7.45 (s, 2H), 7.44 – 7.38 (m, 1H), 7.36 – 7.31 (m, 1H). ¹³C NMR (126 MHz, CDCl₃): δ 181.8, 138.1, 133.8, 132.0, 128.9 (+), 128.2 (+), 126.3 (+), 126.0 (+), 125.9 (+), 125.8 (+), 124.3 (+), 108.8 (+, 2C), 29.1; FT IR (KBr, cm⁻¹): 3161, 3120, 3057, 1691, 1655, 1410, 1310, 1288, 1263, 1236, 1178, 1121, 955, 775, 733, 660, 640; HRMS (TOF ES): Calcd for C₁₄H₁₀O₂Na (M+Na)⁺ 233.0579, Found 233.0590 (4.9 ppm).

1-(2,4-Difluorophenyl)cycloprop-2-ene-1-carboxylic acid (17c)

The titled compound was obtained via typical procedure A from methyl 1-(2,4-difluorophenyl)-2-(trimethylsilyl)cycloprop-2-ene-1-carboxyl-ate (488 mg, 1.73 mmol, 1.00 equiv.) as a pale yellow solid, mp 98.7-101.8 °C, yield 280 mg (1.43 mmol, 86%). ¹H NMR (500 MHz, CDCl₃): δ 7.02 (s, 2H), 6.88 (td, *J* = 8.4, 6.4 Hz, 1H), 6.60 – 6.48 (m, 2H); ¹³C (126 MHz, CDCl₃): δ 180.8, 162.3 (dd, *J* = 248.3, 11.9 Hz), 161.8 (dd, *J* = 249.3, 12.1 Hz), 131.0 (+, dd, *J* = 9.7, 5.6 Hz), 124.6 (dd, *J* = 15.8, 3.8 Hz), 111.3 (+, dd, *J* = 21.3, 3.7 Hz), 107.5 (+, d, *J* = 1.6 Hz, 2C), 104.1 (+, d, *J* = 25.5 Hz), 25.6; FT IR (KBr, cm⁻¹): 3178, 3134, 1693, 1661, 1614, 1504, 1421, 1269, 1138, 1088, 984, 854, 735, 636, 616; HRMS (TOF ES): Calcd for C₁₀H₆F₂O₂Na (M+Na)⁺ 219.0234, Found 219.0223 (4.8 ppm).

1-(2-Chloro-4-fluorophenyl)cycloprop-2-ene-1-carboxylic acid (17d)

The titled compound was obtained via typical procedure using methyl 1-(2-chloro-4-fluorophenyl)-2-(trimethylsilyl)cycloprop-2-ene-1-carboxylate (517 mg, 1.73 mmol, 1.00 equiv.) as a colorless solid, mp 152.4-155.1 °C, yield 303 mg yield (1.43 mmol, 82%). ¹H NMR (500 MHz, CDCl₃): δ 7.30 (s, 2H), 7.18 (dd, *J* = 8.5, 6.0 Hz, 1H), 7.09 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.93 (td, *J* = 8.3, 2.6 Hz, 1H); ¹³C (126 MHz, CDCl₃): δ 180.0, 161.8 (d, *J* = 249.3 Hz), 135.9 (d, *J* = 10.5 Hz), 135.4 (d, *J* = 3.7 Hz), 131.3 (+, d, *J* = 8.7 Hz), 117.0 (+, d, *J* = 24.8 Hz), 114.4 (+, d, *J* = 21.0 Hz), 108.2 (+, 2C), 29.3; FTIR (KBr, cm⁻¹): 3163, 3122, 1693, 1661, 1597, 1585, 1487, 1301, 1238, 1199, 1045, 982, 887, 856, 756, 634; HRMS (TOF ES): Calcd for C₁₀H₆ClFNa (M-H)⁻ 210.9962, Found 210.9958 (1.9 ppm).

N,N-Diethyl-1-phenylcycloprop-2-ene-1-carboxamide (18aa) (typical procedure B)

Flame-dried round bottom flask was charged with 1-phenylcycloprop-2-ene-1-carboxylic acid (**17a**) (250 mg, 1.56 mmol, 1.00 equiv.), DMF (2 drops) and freshly distilled anhydrous dichloromethane (7 ml) under nitrogen atmosphere. Oxalyl chloride (200 μ L, 297 mg, 2.34 mmol, 1.50 equiv.) was then added dropwise and the mixture was stirred at room temperature for 2 h. The solution was concentrated under reduced pressure to provide a pale yellow solid residue, which was dissolved in anhydrous dichloromethane (2.0 mL) and added dropwise to a solution of diethylamine (**20a**) (323 μ L, 228 mg, 3.12 mmol, 2.00 equiv.) and triethylamine (436 μ L, 316 mg, 3.12 mmol, 2.00 equiv.) in anhydrous dichloromethane (3.0 mL). The reaction mixture was stirred for 18 hours at RT and then partitioned between water and dichloromethane. The aqueous phase was acidified with 1N HCl to pH 2. The organic phase was then extracted with acidified water (pH 2, 3 $\times$ 10 mL). The combined aqueous layers were back-extracted once with dichloromethane, which was combined with other organic phases, washed with brine, dried with MgSO₄, filtered, and concentrated. The product was purified by column chromatography on Silica gel eluting

with a 1.5:1 mixture hexane:EtOAc to afford the titled compound as a colorless solid, mp 84.5–86.0 °C, R_f 0.16, yield 300 mg (1.39 mmol, 89%). ^1H NMR (500 MHz, CDCl_3): δ 7.33–7.10 (m, 7H), 3.40 (q, J = 7.0 Hz, 2H), 3.32 (q, J = 7.1 Hz, 2H), 1.17 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3): δ 173.2, 143.5, 128.3 (2C, +), 126.2 (+), 125.9 (2C, +), 109.6 (2C, +), 41.9 (–), 38.9 (–), 32.0, 13.7 (+), 12.6 (+); FT IR (KBr, cm^{-1}): 3078, 2972, 2934, 2872, 1624, 1491, 1472, 1429, 1379, 1364, 1277, 1221, 1121, 1076, 1018, 999, 839, 764, 739, 700, 638; HRMS (TOF ES): HRMS (TOF ES): Calcd for $\text{C}_{14}\text{H}_{17}\text{NO}$ (M^+) 215.1310, Found 215.1311 (0.5 ppm).

***N,N*-Diisopropyl-1-phenylcycloprop-2-ene-1-carboxamide (18ab)**

This compound was obtained via typical procedure **B** employing diisopropylamine (**20b**) (438 μL , 316 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 3:1 mixture hexane:EtOAc to afford a very pale yellow solid, mp 66.9–68.2 °C, R_f 0.26, yield 224 mg (0.92 mmol, 59%). ^1H NMR (500 MHz, CDCl_3): δ 7.24–7.19 (m, 2H), 7.18 (s, 2H), 7.14–7.07 (m, 3H), 4.23 (h, J = 6.7 Hz, 1H), 3.22 (h, J = 6.8 Hz, 1H), 1.40 (d, J = 6.8 Hz, 6H), 0.84 (d, J = 6.7 Hz, 6H); ^{13}C NMR (126 MHz, CDCl_3): δ 173.2, 143.7, 128.3 (+, 2C), 126.3 (+), 126.1 (+, 2C), 110.0 (+, 2C), 49.5 (+), 45.6 (+), 33.5, 20.5 (+, 2C), 20.4 (+, 2C); FT IR (KBr, cm^{-1}): 3080, 3061, 2999, 2966, 2932, 1643, 1626, 1614, 1493, 1435, 1369, 1329, 1213, 1161, 1045, 739, 700, 667, 621; HRMS (TOF ES): Calcd for $\text{C}_{16}\text{H}_{22}\text{NO}$ ($\text{M}+\text{H}^+$) 244.1701, Found 244.1701 (0.0 ppm).

***N,N*-Diallyl-1-phenylcycloprop-2-ene-1-carboxamide (18ac)**

This compound was obtained via typical procedure **B** employing diallylamine (**20c**) (385 μL , 363 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 3:1 mixture hexane:EtOAc to afford a colorless solid, mp 43.1–44.2 °C, R_f 0.22, yield 324 mg (1.35 mmol, 87%). ^1H NMR (500 MHz, CDCl_3): δ 7.25–7.19 (m, 2H), 7.18 (s, 2H), 7.16–7.11 (m, 1H), 7.09–7.05 (m, 2H), 5.74 (ddt, J = 17.1, 10.2, 6.1 Hz, 1H), 5.39 (ddt, J = 17.2, 10.8, 5.4 Hz, 1H), 5.13–4.89 (m, 4H), 3.92 (d, J = 6.1 Hz, 2H), 3.81 (d, J = 5.4 Hz, 2H); ^{13}C NMR (126 MHz, CDCl_3): δ 173.9, 143.2, 133.4 (+), 133.0 (+), 128.5 (+, 2C), 126.5 (+), 126.0 (+, 2C), 117.7 (–), 117.5 (–), 109.6 (+, 2C), 49.5 (–), 46.7 (–), 31.9; FT IR (KBr, cm^{-1}): 3082, 3022, 2982, 2918, 1645, 1634, 1614, 1493, 1447, 1412, 1285, 1248, 995, 926, 764, 733, 700; HRMS (TOF ES): Calcd for $\text{C}_{16}\text{H}_{18}\text{NO}$ ($\text{M}+\text{H}^+$) 240.1388, Found 240.1387 (0.4 ppm).

***N,N*-Dibenzyl-1-phenylcycloprop-2-ene-1-carboxamide (18ad)**

This compound was obtained via typical procedure **B** employing dibenzylamine (**20d**) (600 μL , 616 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 3:1 mixture hexane:EtOAc to afford a colorless solid, mp 112.3–113.9 °C, R_f 0.30; yield 402 mg (1.18 mmol, 76%). ^1H NMR (500 MHz, CDCl_3): δ 7.27–7.13 (m, 10H), 7.12–7.07 (m, 1H), 7.05 (s, 2H), 7.05–7.02 (m, 2H), 6.88–6.84 (m, 2H), 4.47 (s, 2H), 4.31 (s, 2H); ^{13}C NMR (126 MHz, CDCl_3): δ 174.6, 143.1, 137.3, 136.9, 128.9 (+, 2C), 128.8 (+, 2C), 128.7 (+, 2C), 128.6 (+, 2C), 127.6 (+), 127.6 (+), 127.0 (+, 2C), 126.6 (+), 126.1 (+, 2C), 109.8 (+, 2C), 50.2 (–), 47.5 (–), 32.0; FT IR (KBr, cm^{-1}): 3084, 3061, 3028, 2924, 2870, 1645, 1634, 1495, 1452, 1418, 1229, 1080, 957, 752, 735,

698, 654; HRMS (TOF ES): Calcd for $C_{24}H_{22}NO$ (M+H)⁺ 340.1701, Found 340.1701 (0.0 ppm).

***N*-Benzyl-*N*-methyl-1-phenylcycloprop-2-ene-1-carboxamide (18ae)**

This compound was obtained via typical procedure **B** employing *N*-methylbenzylamine (**20e**) (403 μ L, 378 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 3:1 mixture hexane:EtOAc to afford a mixture of rotamers in a ratio of 1.3:1 as a colorless oil, R_f 0.15, yield 362 mg (1.37 mmol, 88%). ¹H NMR (500 MHz, CDCl₃): δ [7.36 – 7.11 (m), Σ 10H], [7.29, (s) & 7.14 (s), Σ 2H], [4.63 (s) & 4.51 (s), Σ 2H], [2.92 (s) & 2.80 (s), Σ 3H]; ¹³C NMR (126 MHz, CDCl₃): δ Major rotamer: 174.0, 143.0, 137.3, 128.6 (+, 2C), 128.5 (+, 2C), 128.2 (+, 2C), 127.4 (+), 126.3 (+), 125.9 (+, 2C), 109.4 (+, 2C), 50.7 (–), 34.9 (+), 32.1. Minor rotamer: 174.6, 143.1, 136.8, 128.8 (+, 2C), 128.5 (+, 2C), 127.5 (+), 126.7 (+, 2C), 126.5 (+), 125.9 (+, 2C), 109.4 (+, 2C), 53.6 (–), 33.1 (+), 31.8; FT IR (KBr, cm^{–1}): 3084, 3028, 2920, 1645, 1614, 1489, 1447, 1398, 1269, 1101, 1003, 959, 739, 698, 652; HRMS (TOF ES): Calcd for $C_{18}H_{18}NO$ (M+H)⁺ 264.1388, Found 264.1392 (1.4 ppm).

***N*-Benzyl-*N*-isopropyl-1-phenylcycloprop-2-ene-1-carboxamide (18af)**

This compound was obtained via typical procedure **B** employing *N*-isopropylbenzylamine (**20f**) (522 μ L, 466 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 3:1 mixture hexane:EtOAc to afford a mixture of rotamers in a ratio of 1.3:1 as a colorless solid, mp 58.7–60.3 °C, R_f 0.23, yield 363 mg (1.25 mmol, 80%). ¹H NMR (500 MHz, CDCl₃): δ [7.33 (s) & 6.83 (s), Σ 2H], [7.32 – 7.27 (m), Σ 5H], [7.25 – 7.17 (m), Σ 3H] [7.11 – 7.01 (m), Σ 2H], [4.69 (h, J = 6.8 Hz) & 4.48 (h, J = 6.7 Hz), Σ 1H], [4.52 (s) & 4.37 (s), Σ 2H], [1.16 (d, J = 6.8 Hz) & 0.92 (d, J = 6.8 Hz), Σ 6H]; ¹³C NMR (126 MHz, CDCl₃): δ Major rotamer: 174.4, 143.4, 139.9, 128.5 (+, 2C), 128.4 (+, 2C), 127.5 (+, 2C), 126.7 (+), 126.5 (+), 126.2 (+, 2C), 110.2 (+, 2C), 49.3 (+), 43.9 (–), 32.4, 21.4 (+, 2C). Minor rotamer: 174.7, 143.4, 139.5, 128.6 (+, 2C), 128.5 (+, 2C), 127.2 (+), 126.6 (+, 2C), 126.4 (+), 125.9 (+, 2C), 109.3 (+, 2C), 47.7 (–), 47.1 (+), 32.8, 20.3 (+, 2C); FT IR (KBr, cm^{–1}): 3082, 3061, 3026, 2972, 2932, 1626, 1495, 1437, 1412, 1339, 1178, 1078, 735, 698, 652; HRMS (TOF ES): Calcd for $C_{20}H_{22}NO$ (M+H)⁺ 292.1701, Found 292.1692 (3.2 ppm).

***N*-Benzyl-*N*-cyclohexyl-1-phenylcycloprop-2-ene-1-carboxamide (18ag)**

This compound was obtained via typical procedure **B** employing *N*-cyclohexylbenzylamine (**20g**) (591 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 3:1 mixture hexane:EtOAc to afford a mixture of rotamers in a ratio of 1.5:1 as a very pale-yellow oil, R_f 0.27, yield 432 mg (1.30 mmol, 84%). ¹H NMR (500 MHz, CDCl₃): δ [7.35 (s) & 6.80 (s), Σ 2H], [7.32 – 7.27 (m), Σ 5H], [7.25 – 7.18 (m), Σ 3H], [7.09 – 7.00 (m), Σ 2H], [4.52 (s) & 4.40 (s), Σ 2H], [4.46 – 4.40 (m) & 4.07 – 3.97 (m), Σ 1H], [1.82 – 1.69 (m) & 1.65 – 1.56 (m) & 1.52 – 1.44 (m) & 1.40 – 1.22 (m) & 1.08 – 0.84 (m), Σ 10H]; ¹³C NMR (126 MHz, CDCl₃): δ Major rotamer: 174.6, 143.5, 139.9, 128.5 (+, 2C), 128.3 (+, 2C), 127.5 (+, 2C), 126.7 (+), 126.6 (+), 126.3 (+, 2C), 110.7 (+, 2C), 58.1 (+), 44.9 (–), 32.6, 32.1 (–, 2C), 26.1 (–, 2C), 25.3 (–). Minor

rotamer: 174.7, 143.5, 139.8, 128.5, 128.5, 127.1, 126.6, 126.4, 125.9, 109.2, 54.9, 47.9, 32.7, 30.6, 26.0, 25.6; FT IR (KBr, cm^{-1}): 3082, 3060, 3028, 2930, 2854, 1645, 1625, 1607, 1495, 1447, 1416, 1244, 1078, 1003, 912, 737, 698, 656; HRMS (TOF ES): Calcd for $\text{C}_{23}\text{H}_{26}\text{NO}$ ($\text{M}+\text{H}$)⁺ 332.2014, Found 332.2015 (0.2 ppm).

(1-Phenylcycloprop-2-en-1-yl)(pyrrolidin-1-yl)methanone (18ai)

This compound was obtained via typical procedure **B** employing pyrrolidine (**20i**) (256 μL , 222 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 2:1 mixture hexane:EtOAc to afford a colorless solid, mp 140.7–143.6 $^{\circ}\text{C}$, R_f 0.10, yield 279 mg (1.31 mmol, 84%). ^1H NMR (500 MHz, CDCl_3): δ 7.25–7.20 (m, 2H), 7.20 (s, 2H), 7.15–7.10 (m, 1H), 7.09–7.05 (m, 2H), 3.45 (dd, J = 7.2, 6.2 Hz, 2H), 3.15 (dd, J = 6.4 Hz, 2H), 1.79–1.67 (m, 4H); ^{13}C NMR (126 MHz, CDCl_3): δ 172.4, 143.0, 128.5 (+, 2C), 126.3 (+), 126.2 (+, 2C), 109.3 (+, 2C), 46.6 (–), 45.9 (–), 32.9, 26.1 (–), 24.2 (–); FT IR (KBr, cm^{-1}): 3103, 3057, 2968, 2872, 1616, 1447, 1431, 1045, 914, 731, 681, 669; HRMS (TOF ES): Calcd for $\text{C}_{14}\text{H}_{16}\text{NO}$ ($\text{M}+\text{H}$)⁺ 214.1232, Found 214.1234 (0.9 ppm).

(1-Phenylcycloprop-2-en-1-yl)(piperidin-1-yl)methanone (18j)

This compound was obtained via typical procedure **B** employing piperidine (**20j**) (308 μL , 266 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 2:1 mixture hexane:EtOAc to afford a colorless solid, mp 128.6–132.5 $^{\circ}\text{C}$, R_f 0.26, yield 295 mg (1.30 mmol, 83%). ^1H NMR (500 MHz, CDCl_3): δ 7.31–7.24 (m, 2H), 7.22 (s, 2H), 7.20–7.16 (m, 1H), 7.14–7.11 (m, 2H), 3.63–3.51 (m, 2H), 3.46–3.22 (m, 2H), 1.69–1.45 (m, 4H), 1.36–1.18 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3): δ 172.3, 143.5, 128.4 (+, 2C), 126.2 (+), 125.9 (+, 2C), 109.2 (+, 2C), 47.0 (–), 42.7 (–), 31.8, 26.0 (–), 25.5 (–), 24.5 (–); FT IR (KBr, cm^{-1}): 3103, 3059, 3016, 2943, 2916, 2851, 1618, 1439, 1269, 1256, 1122, 1043, 974, 910, 852, 760, 739, 696, 681; HRMS (TOF ES): Calcd for $\text{C}_{15}\text{H}_{18}\text{NO}$ ($\text{M}+\text{H}$)⁺ 228.1388, Found 228.1386 (0.9 ppm).

Morpholino(1-phenylcycloprop-2-en-1-yl)methanone (18k)

This compound was obtained via typical procedure **B** employing morpholine (**20k**) (270 μL , 272 mg, 3.12 mmol, 2.0 equiv.). The product was purified by column chromatography on Silica gel eluting with a 2:1 mixture hexane:EtOAc to afford a colorless solid, mp 115.1–117.6 $^{\circ}\text{C}$, R_f 0.13, yield 340 mg (1.48 mmol, 95%). ^1H NMR (500 MHz, CDCl_3): δ 7.32–7.27 (m, 2H), 7.23 (s, 2H), 7.22–7.17 (m, 1H), 7.14–7.09 (m, 2H), 3.65 (s, 4H), 3.39 (s, 4H); ^{13}C NMR (126 MHz, CDCl_3): δ 172.7, 142.9, 128.6 (+, 2C), 126.6 (+), 125.8 (+, 2C), 108.9 (+, 2C), 66.8 (–), 66.5 (–), 46.4 (–), 42.1 (–), 31.5; FT IR (KBr, cm^{-1}): 3105, 3063, 2966, 2916, 2856, 1626, 1429, 1273, 1248, 1115, 980, 766, 737, 702; HRMS (TOF ES): Calcd for $\text{C}_{14}\text{H}_{16}\text{NO}_2$ ($\text{M}+\text{H}$)⁺ 230.1181, Found 230.1197 (6.9 ppm).

(4-Ethylpiperazin-1-yl)(1-phenylcycloprop-2-en-1-yl)methanone (18l) (typical procedure C)

This compound was obtained via typical procedure **B** employing 1-ethylpiperazine (**20l**) (396 μL , 356 mg, 3.12 mmol, 2.00 equiv.). Alterations were incorporated into isolation and purification protocols. After partitioning of the crude mixture between water and

dichloromethane the aqueous phase was acidified with 1N HCl to pH 2. The organic phase was extracted with dilute HCl (pH 2, 3 × 15 mL). The combined aqueous phases were basified to pH 9 with saturated aqueous sodium carbonate solution and extracted with dichloromethane (3 × 15 mL). The combined organic phase was then washed with brine, dried, filtered, and concentrated. The product was then purified by column chromatography on Silica gel doped with triethylamine eluting with EtOAc. The titled compound was afforded as a colorless solid, mp 51.9-53.7 °C, R_f 0.17, yield 361 mg (1.41 mmol, 90%). ^1H NMR (500 MHz, CDCl_3): δ 7.29 – 7.23 (m, 2H), 7.20 (s, 2H), 7.19 – 7.14 (m, 1H), 7.11 – 7.07 (m, 2H), 3.70 – 3.61 (m, 2H), 3.45 – 3.37 (m, 2H), 2.44 – 2.36 (m, 2H), 2.33 (q, J = 7.2 Hz, 2H), 2.19 – 2.08 (m, 2H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3): δ 172.4, 143.1, 128.4 (+, 2C), 126.4 (+), 125.9 (+, 2C), 108.9 (+, 2C), 52.6 (–), 52.4 (–), 52.2 (–), 45.8 (–), 41.6 (–), 31.6, 11.9 (+); FT IR (KBr, cm^{-1}): 3080, 2968, 2931, 2808, 1628, 1437, 1252, 1167, 1124, 1022, 982, 764, 737, 700, 652; HRMS (TOF ES): Calcd for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^+$ 257.1654, Found 257.1648 (2.3 ppm).

***N*-Butyl-1-phenylcycloprop-2-ene-1-carboxamide (18am)**

This compound was obtained via typical procedure **B** employing *n*-butylamine (**20m**) (308 μL , 228 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc to afford a colorless solid, mp 48.2-50.1 °C, R_f 0.32, yield 284 mg (1.32 mmol, 85%). ^1H NMR (500 MHz, CDCl_3): δ 7.35 – 7.21 (m, 5H), 7.25 (s, 2H), 5.60 (s, 1H), 3.21 (td, J = 7.2, 5.8 Hz, 2H), 1.48 – 1.31 (m, 2H), 1.31 – 1.15 (m, 2H), 0.86 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3): δ 174.8, 142.0, 128.8 (+, 2C), 128.6 (+, 2C), 127.1 (+), 108.9 (+, 2C), 39.9 (–), 32.6, 31.7 (–), 20.0 (–), 13.8 (+); FT IR (KBr, cm^{-1}): 3277, 3082, 2952, 2927, 2858, 1623, 1541, 1431, 1308, 1224, 1143, 1012, 743, 694, 689; HRMS (TOF ES): Calcd for $\text{C}_{14}\text{H}_{18}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 216.1388, Found 216.1396 (3.5 ppm).

***N*-Cycloheptyl-1-phenylcycloprop-2-ene-1-carboxamide (18an)**

This compound was obtained via typical procedure **B** employing cycloheptylamine (**20n**) (397 μL , 353 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc to afford a colorless solid, mp 118.9-120.8 °C, R_f 0.42, yield 321 mg (1.26 mmol, 81%). ^1H NMR (500 MHz, CDCl_3): δ 7.35 – 7.22 (m, 5H), 7.25 (s, 2H), 5.52 (d, J = 7.7 Hz, 1H), 4.07 – 3.81 (m, 1H), 1.90 – 1.76 (m, 2H), 1.62 – 1.37 (m, 8H), 1.38 – 1.27 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3): δ 173.6, 142.1, 128.8 (+, 2C), 128.7 (+, 2C), 127.1 (+), 108.9 (+, 2C), 50.9 (+), 35.0 (–, 2C), 32.7, 27.9 (–, 2C), 24.1 (–, 2C); FT IR (KBr, cm^{-1}): 3294, 3136, 3084, 2914, 2853, 1614, 1531, 1445, 1319, 1627, 1334, 1009, 739, 696, 667; HRMS (TOF ES): Calcd for $\text{C}_{17}\text{H}_{22}\text{NO}$ ($\text{M}+\text{H}$) $^+$ 256.1701, Found 256.1702 (0.2 ppm).

***N*-Allyl-1-phenylcycloprop-2-ene-1-carboxamide (18ao)**

This compound was obtained via typical procedure **B** employing allylamine (**20o**) (233 μL , 178 mg, 3.12 mmol, 2.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc to afford a colorless solid, mp 68.0-69.1 °C, R_f 0.27, yield 286 mg (1.44 mmol, 92%). ^1H NMR (500 MHz, CDCl_3): δ

7.38 – 7.21 (m, 5H), 7.28 (s, 2H), 5.78 (ddt, J = 17.3, 10.6, 5.5 Hz, 1H), 5.68 (s, 1H), 5.15 – 5.00 (m, 2H), 3.91 – 3.82 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3): δ 174.8, 141.8, 134.4 (+), 128.9 (+, 2C), 128.7 (+, 2C), 127.3 (+), 116.0 (–), 108.9 (+, 2C), 42.5 (–), 32.6; FT IR (KBr, cm^{-1}): 3279, 3080, 2927, 1626, 1529, 1425, 1265, 1146, 1013, 986, 916, 741, 694; HRMS (TOF ES): Calcd for $\text{C}_{13}\text{H}_{14}\text{NO}$ ($\text{M}+\text{H}$) $^{+}$ 200.1075, Found 200.1077 (0.8 ppm).

1-Phenyl-*N*-(prop-2-yn-1-yl)cycloprop-2-ene-1-carboxamide (18ap)

This compound was obtained via typical procedure **B** employing propargylamine (**20p**) (200 μL , 172 mg, 3.12 mmol, 2.0 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc to afford a colorless solid mp 123.8–124.7 $^{\circ}\text{C}$, R_f 0.33, yield 219 mg (1.11 mmol, 71%). ^1H NMR (500 MHz, CDCl_3): δ 7.41 – 7.36 (m, 2H), 7.34 – 7.28 (m, 3H), 7.31 (s, 2H), 5.78 (s, 1H), 4.07 (dd, J = 5.4, 2.6 Hz, 2H), 2.20 (t, J = 2.6 Hz, 1H); ^{13}C NMR (126 MHz, CDCl_3): δ 174.8, 141.4, 129.1 (+, 2C), 128.8 (+, 2C), 127.5 (+), 108.7 (+, 2C), 79.8 (+), 71.5, 32.5, 29.9 (–). FT IR (KBr, cm^{-1}): 3319, 3286, 3134, 3090, 1655, 1630, 1524, 1423, 1360, 1277, 1005, 930, 854, 744, 675, 635; HRMS (TOF ES): Calcd for $\text{C}_{13}\text{H}_{12}\text{NO}$ ($\text{M}+\text{H}$) $^{+}$ 198.0919, Found 198.0922 (1.6 ppm).

1-Phenyl-*N*-(pyridin-2-ylmethyl)cycloprop-2-ene-1-carboxamide (18aq)

This compound was obtained via typical procedure **C** employing 2-(aminomethyl)pyridine (**20q**) (322 μL , 337 mg, 3.12 mmol, 2.0 equiv.). The product was purified by column chromatography on Silica gel doped with triethylamine eluting with a 1:3 mixture hexane:EtOAc to afford a colorless solid, mp 97.7–100.2 $^{\circ}\text{C}$, R_f 0.23, yield 349 mg (1.39 mmol, 89%). ^1H NMR (500 MHz, CDCl_3): δ 8.53 – 8.40 (m, 1H), 7.75 – 7.63 (m, 1H), 7.37 – 7.26 (m, 6H), 7.33 (s, 2H), 7.23 – 7.19 (m, 1H), 6.82 (s, 1H), 4.58 (d, J = 5.4 Hz, 2H); ^{13}C NMR (126 MHz, CDCl_3): δ 175.4, 156.7, 148.3 (+), 141.7, 137.7 (+), 128.9 (+, 2C), 128.8 (+, 2C), 127.3 (+), 122.7 (+), 122.6, 109.1 (+, 2C), 45.0 (–), 32.5; FT IR (KBr, cm^{-1}): 3290, 3084, 3061, 1660, 1643, 1634, 1514, 1494, 1435, 1296, 1252, 995, 756, 700, 667; HRMS (TOF ES): Calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^{+}$ 251.1184, Found 251.1185 (0.2 ppm).

N-(furan-2-ylmethyl)-1-phenylcycloprop-2-ene-1-carboxamide (18ar)

This compound was obtained via typical procedure **B** employing furfurylamine (**20r**) (276 μL , 303 mg, 3.12 mmol, 2.0 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc to afford a colorless solid, mp 51.4–54.1 $^{\circ}\text{C}$, R_f 0.33, yield 286 mg (1.20 mmol, 77%). ^1H NMR (500 MHz, CDCl_3): δ 7.36 – 7.22 (m, 6H), 7.27 (s, 2H), 6.28 (dd, J = 3.2, 1.9 Hz, 1H), 6.16 (dd, J = 3.2, 0.9 Hz, 1H), 5.92 (t, J = 5.7 Hz, 1H), 4.43 (dd, J = 5.6, 0.8 Hz, 2H); ^{13}C NMR (126 MHz, CDCl_3): δ 174.8, 151.6, 142.1 (+), 141.6, 128.9 (+, 2C), 128.7 (+, 2C), 127.3 (+), 110.4 (+), 108.8 (+, 2C), 107.2 (+), 37.2 (–), 32.6. FT IR (KBr, cm^{-1}): 3292, 3107, 3082, 3057, 1637, 1504, 1445, 1294, 1229, 1148, 1076, 1007, 741, 700, 663; HRMS (TOF ES): Calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_2$ ($\text{M}+\text{H}$) $^{+}$ 240.1025, Found 240.1026 (0.4 ppm).

***N*-(2-Hydroxyethyl)-1-phenylcycloprop-2-ene-1-carboxamide (18as)**

This compound was obtained via typical procedure **B** employing ethanolamine (**20s**) (189 μ l, 190 mg, 3.12 mmol, 2.0 equiv.). The product was purified by column chromatography on Silica gel eluting with EtOAc to afford a colorless oil, R_f 0.17, yield 138 mg (0.68 mmol, 44%). ^1H NMR (500 MHz, CDCl_3): δ 7.17 – 7.05 (m, 5H), 7.08 (s, 2H), 5.92 (s, 1H), 3.44 (t, J = 5.5 Hz, 2H), 3.18 (td, J = 5.7, 4.4 Hz, 2H), 2.88 (s, 1H); ^{13}C NMR (126 MHz, CDCl_3): δ 176.7, 141.5, 129.0 (+, 2C), 128.8 (+, 2C), 127.4 (+), 108.9 (+, 2C), 62.7 (–), 43.3 (–), 32.5; FT IR (KBr, cm^{-1}): 3340, 3103, 2934, 2876, 1660, 1643, 1614, 1537, 1518, 1445, 1240, 1072, 991, 764, 700, 665; HRMS (TOF ES): Calcd for $\text{C}_{12}\text{H}_{14}\text{NO}_2$ ($\text{M} + \text{H}$) $^+$ 204.1025, Found 204.1030 (2.7 ppm).

1-Phenylcycloprop-2-ene-1-carboxamide (18at)

This compound was obtained via modified procedure **B**. Generated crude acyl chloride was dissolved in dry THF (3 mL), then added dropwise to a 30% aqueous ammonia (5 mL), and stirred overnight. The mixture was concentrated in vacuum, diluted with water (10 mL), and extracted with EtOAc (3 $\times$ 10 mL). Combined organic phases were washed with brine, dried with MgSO_4 , filtered, and concentrated. The product was purified by column chromatography on Silica gel eluting with EtOAc to afford a colorless solid mp 118.2–119.0 $^\circ\text{C}$, R_f 0.23, yield 171 mg (1.07 mmol, 69%). ^1H NMR (500 MHz, CDCl_3): δ 7.32 – 7.16 (m, 5H), 7.22 (s, 2H), 5.98 (s, 1H), 5.54 (s, 1H); ^{13}C NMR (126 MHz, CDCl_3): δ 178.0, 141.7, 129.0 (+, 2C), 128.7 (+, 2C), 127.4 (+), 108.7 (+, 2C), 32.2; FT IR (KBr, cm^{-1}): 3362, 3188, 3111, 1608, 1402, 1261, 1113, 993, 760, 737, 696, 642; HRMS (TOF ES): Calcd for $\text{C}_{10}\text{H}_{10}\text{NO}$ ($\text{M} + \text{H}$) $^+$ 160.0762, Found 160.0754 (5.0 ppm).

***N*-Methoxy-*N*-methyl-1-phenylcycloprop-2-ene-1-carboxamide (18au)**

This compound was obtained via typical procedure **B** employing *N,N*-dimethylhydroxylamine (**20u**) (228 mg, 2.34 mmol, 1.50 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc to afford a colorless solid, MP: 74.3–75.6 $^\circ\text{C}$, R_f 0.30, yield 262 mg (1.29 mmol, 83%). ^1H NMR (500 MHz, CDCl_3): δ 7.29 (s, 2H), 7.28 – 7.25 (m, 2H), 7.22 – 7.13 (m, 3H), 3.30 (s (broad), 3H), 3.15 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3): δ 175.3, 143.2, 128.3 (+, 2C), 126.3 (+, 3C), 109.9 (+, 2C), 60.7 (+), 32.8, 31.7 (+); FT IR (KBr, cm^{-1}): 3080, 3018, 2972, 2937, 1649, 1624, 1491, 1423, 1387, 1200, 1026, 966, 756, 729, 702, 648; HRMS (TOF ES): Calcd for $\text{C}_{12}\text{H}_{14}\text{NO}_2$ ($\text{M} + \text{H}$) $^+$ 204.1025, Found 204.1031 (3.2 ppm).

***N,N*-(Ethane-1,2-diyl)bis(1-phenylcycloprop-2-ene-1-carboxamide) (21)**

This compound was obtained via modified procedure **B** employing 1,2-ethylenediamine (417 μ l, 375 mg, 6.24 mmol, 4.0 equiv.). In this instance excess ethylenediamine was used as a base in place of triethylamine. The product displaying poor solubility in most of common solvents was purified by recrystallization from EtOAc to provide the titled compound as a colorless solid, mp 186–190 $^\circ\text{C}$ (dec), yield 150 mg, (0.44 mmol, 56%). ^1H NMR (500 MHz, CDCl_3): δ 7.38 – 7.25 (m, 10H), 7.24 (s, 4H), 5.99 (s, 2H), 3.33 (d, J = 5.6 Hz, 4H); ^{13}C NMR (126 MHz, CDCl_3): δ 175.9 (2C), 141.7 (2C), 129.0 (+, 4C), 128.7 (+, 4C), 127.4 (+, 2C), 109.0 (+, 4C), 40.3 (–, 2C), 32.5 (2C); FTIR (KBr, cm^{-1}): 3323, 3146, 3107, 1659,

1633, 1514, 1286, 1261, 1224, 1001, 984, 768, 702, 667, 608; HRMS (TOF ES): Calcd for $C_{22}H_{21}N_2O_2$ (M+H)⁺ 345.1603, Found 345.1604 (0.3 ppm).

***N,N*-Diethyl-1-(naphthalen-2-yl)cycloprop-2-ene-1-carboxamide (18ba)**

This compound was obtained via typical procedure **B** employing 1-(naphthalen-2-yl)cycloprop-2-ene-1-carboxylic acid (**17b**) (85.0 mg, 0.404 mmol, 1.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane:EtOAc to afford a colorless solid, mp 123.8–125.5 °C, *R*_f 0.33, yield 98.0 mg (0.370 mmol, 92%). ¹H NMR (500 MHz, CDCl₃): δ 8.32–8.24 (m, 1H), 7.66–7.60 (m, 1H), 7.56–7.50 (m, 1H), 7.40 (s, 2H), 7.35–7.19 (m, 3H), 7.10–7.03 (m, 1H), 3.10 (q, *J* = 7.1 Hz, 2H), 3.04 (q, *J* = 7.1 Hz, 2H), 0.79 (t, *J* = 7.1 Hz, 3H), 0.13 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃): δ 174.9, 141.0, 133.7, 132.7, 128.5 (+), 127.6 (+), 126.4 (+), 126.0 (+), 125.9 (+), 125.8 (+), 125.3 (+), 112.0 (+, 2C), 42.3 (+), 40.7 (+), 32.6, 13.0 (+), 12.8 (+); FT IR (KBr, cm⁻¹): 3074, 2974, 2931, 2872, 1614, 1454, 1427, 1271, 781, 667, 631; HRMS (TOF ES): Calcd for C₁₈H₁₉NONa (M+Na)⁺ 288.1364, Found 288.1364 (0.0 ppm).

1-(2,4-Difluorophenyl)-*N,N*-diethylcycloprop-2-ene-1-carboxamide (18ca)

This compound was obtained via typical procedure **B** employing 1-(2,4-difluorophenyl)cycloprop-2-ene-1-carboxylic acid (**17c**) (163 mg, 0.831 mmol, 1.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane: EtOAc to afford an off-white solid, mp 59.7–60.8 °C, *R*_f 0.22, yield 178 mg (0.708 mmol, 85%). ¹H NMR (500 MHz, CDCl₃): δ 7.34 (s, 2H), 7.16 (td, *J* = 8.8, 6.4 Hz, 1H), 6.84–6.78 (m, 1H), 6.77–6.72 (m, 1H), 3.44–3.23 (m, 4H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.78 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃): δ 173.0, 161.7 (dd, *J* = 248.3, 11.9 Hz), 161.2 (dd, *J* = 249.8, 11.8 Hz), 130.4 (+, dd, *J* = 9.6, 5.5 Hz), 126.8 (dd, *J* = 12.6, 3.8 Hz), 111.4 (+, dd, *J* = 21.1, 3.7 Hz), 110.3 (+, d, *J* = 1.9 Hz, 2C), 104.2 (+, t, *J* = 25.6 Hz), 41.7 (–), 39.6 (–), 27.8, 13.3 (+), 12.5 (+); FT IR (KBr, cm⁻¹): 3080, 2976, 2935, 2876, 1625, 1500, 1421, 1267, 1140, 1092, 974, 847, 623; HRMS (TOF ES): Calcd for C₁₄H₁₆F₂NO (M+H)⁺ 252.1200, Found 252.1200 (0.0 ppm).

1-(2-Chloro-4-fluorophenyl)-*N,N*-diethylcycloprop-2-ene-1-carboxamide (18da)

This compound was obtained via typical procedure **B** employing 1-(2-chloro-4-fluorophenyl)cycloprop-2-ene-1-carboxylic acid (**17d**) (267 mg, 1.26 mmol, 1.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane: EtOAc to afford a colorless solid, mp 81.1–82.6 °C, *R*_f 0.27, yield 277 mg (1.03 mmol, 83%). ¹H NMR (500 MHz, CDCl₃): δ 7.28 (s, 2H), 7.25–7.19 (m, 1H), 6.98 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.88 (ddd, *J* = 8.7, 7.8, 2.6 Hz, 1H), 3.25 (q, *J* = 7.1 Hz, 4H), 1.03 (t, *J* = 7.2 Hz, 3H), 0.62 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃): δ 173.1, 161.2 (d, *J* = 249.5 Hz), 137.2 (d, *J* = 3.6 Hz), 134.4 (d, *J* = 10.1 Hz), 131.7 (+, d, *J* = 8.7 Hz), 117.2 (+, d, *J* = 24.3 Hz), 114.4 (+, d, *J* = 21.0 Hz), 110.1 (+, 2C), 41.8 (–), 40.2 (–), 31.5, 13.1 (+), 12.6 (+); FT IR (KBr, cm⁻¹): 3121, 3084, 2980, 2968, 2934, 1616, 1483, 1385, 1244, 1217, 1194, 1045, 889, 870, 652, 633; HRMS (TOF ES): Calcd for C₁₄H₁₆ClFNO (M+H)⁺ 268.0904, Found 268.0905 (0.2 ppm).

***N,N*-Diethyl-1,2-diphenylcycloprop-2-ene-1-carboxamide (3a)**

This compound was obtained via typical procedure **B** employing 1,2-diphenylcycloprop-2-ene-1-carboxylic acid (**2a**) (400 mg, 1.69 mmol, 1.0 equiv.). The product was purified by column chromatography on Silica gel eluting with a 1:1 mixture hexane: EtOAc to afford a yellow oil, *R_f* 0.53, yield 458 mg (1.57 mmol, 93%). ¹H NMR (500 MHz, CDCl₃): δ 7.89 – 7.71 (m, 2H), 7.41 – 7.29 (m, 7H), 7.23 – 7.18 (m, 1H), 7.14 (s, 1H), 3.72 – 3.47 (m, 2H), 3.41 – 3.26 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.1 Hz, 3H); ¹³C (126 MHz, CDCl₃): δ 173.1, 142.6, 130.3 (+, 2C), 129.6 (+), 128.6 (+, 2C), 128.4 (+, 2C), 126.3, 126.2 (+), 126.0 (+, 2C), 122.3, 98.7 (+), 42.1 (–), 38.9 (–), 35.4, 13.7 (+), 12.6 (+). FT IR (KBr, cm^{–1}): 3080, 3059, 2974, 2933, 2873, 1682, 1614, 1445, 1427, 1381, 1277, 1221, 1072, 922, 768, 698, 644; HRMS (TOF ES): Calcd for C₂₀H₂₂NO (M+H)⁺ 292.1701, Found 292.1699 (0.8 ppm).

***2*-Butyl-*N,N*-diethyl-1-phenylcycloprop-2-ene-1-carboxamide (3b)**

This compound was obtained via typical procedure **B** employing 2-butyl-1-phenylcycloprop-2-enecarboxylic (**2b**) (450 mg, 2.08 mmol, 1.00 equiv.). The product was purified by column chromatography on Silica gel eluting with a 3:1 mixture hexane: EtOAc to afford a pale yellow oil, *R_f* 0.34, yield 434 mg (1.60 mmol, 80%). ¹H NMR (500 MHz, CDCl₃): δ 7.23 – 7.16 (m, 2H), 7.12 – 7.01 (m, 3H), 6.59 (s, 1H), 3.45 (dq, *J* = 14.0, 7.1 Hz, 1H), 3.29 (dq, *J* = 14.3, 7.1 Hz, 1H), 3.16 (dq, *J* = 14.4, 7.3 Hz, 2H), 2.63 – 2.45 (m, 2H), 1.59 – 1.42 (m, 2H), 1.35 – 1.18 (m, 2H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.79 (q, *J* = 7.1 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃): δ 174.1, 143.9, 128.3 (+ 2C), 125.9 (+, 2C), 125.8 (+), 124.2, 98.2 (+), 41.9 (–), 38.7 (–), 34.2, 29.2 (–), 24.2 (–), 22.4 (–), 13.8 (+), 13.6 (+), 12.7 (+); FT IR (KBr, cm^{–1}): 3082, 3057, 2961, 2932, 2972, 1643, 1634, 1614, 1493, 1445, 1423, 1379, 1275, 1221, 1099, 856, 700; HRMS (TOF ES): Calcd for C₁₈H₂₆NO (M+H)⁺ 272.2014, Found 272.2019 (1.8 ppm).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Scheme 1.

Scheme 2.

2a, 3a: R = Ph, 93%
2b, 3b: R = *n*-Bu, 80%

Scheme 3.

Scheme 4.

Table 1

Synthesis of 1-arylcycloprop-2-ene-1-carboxamides.

#	17	20	18	R ¹	R ²	R ³	Yield, % ^a
1	17a	20a	18aa	Ph	Et	Et	89
2	17a	20b	18ab	Ph	<i>i</i> -Pr	<i>i</i> -Pr	59
3	17a	20c	18ac	Ph	CH ₂ CH=CH ₂	CH ₂ CH=CH ₂	87
4	17a	20d	18ad	Ph	CH ₂ Ph	CH ₂ Ph	76
5	17a	20e	18ae	Ph	CH ₂ Ph	Me	88
6	17a	20f	18af	Ph	CH ₂ Ph	<i>i</i> -Pr	80
7	17a	20g	18ag	Ph	CH ₂ Ph	Cy	84
8	17a	20h	18ah	Ph	Ph	Ph	0
9	17a	20i	18ai	Ph	-(CH ₂) ₄ -		84
10	17a	20j	18aj	Ph	-(CH ₂) ₅ -		83
11	17a	20k	18ak	Ph	-(CH ₂) ₂ O(CH ₂) ₂ -		95
12	17a	20l	18al	Ph	-(CH ₂) ₂ NEt(CH ₂) ₂ -		90
13	17a	20m	18am	Ph	<i>n</i> -Bu	H	85
14	17a	20n	18an	Ph	<i>c</i> -heptyl	H	81
15	17a	20o	18ao	Ph	CH ₂ CH=CH ₂	H	92
16	17a	20p	18ap	Ph	CH ₂ C≡CH	H	71
17	17a	20q	18aq	Ph	2-Pic ^b	H	89
18	17a	20r	18ar	Ph	2-Fur ^c	H	77
19	17a	20s	18as	Ph	CH ₂ CH ₂ OH	H	44
20	17a	20t	18at	Ph	H	H	69
21	17a	20u	18au	Ph	Me	OMe	83
22	17b	20a	18ba	1-Npth ^d	Et	Et	92
23	17c	20a	18ca	2,4-F ₂ C ₆ H ₃	Et	Et	85
24	17d	20a	18da	2-Cl-4-FC ₆ H ₃	Et	Et	83

^aIsolated yields of purified products are listed.^b2-Picolyl (pyridine-2-ylmethyl).^cFurfuryl (furan-2-ylmethyl).^d1-Naphthyl.