Tetrahedron 66 (2010) 4947–4953

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

# Ring-retentive deprotonation of cyclopropene-3-carboxamides

Ryan Kim, William M. Sherrill, Michael Rubin *

*Department of Chemistry, University of Kansas, 1251 Wescoe Hall Drive, Lawrence, KS 66045-758, USA*

ARTICLE INFO

*Article history:*
Received 10 December 2009
Received in revised form 27 April 2010
Accepted 28 April 2010
Available online 4 May 2010

ABSTRACT

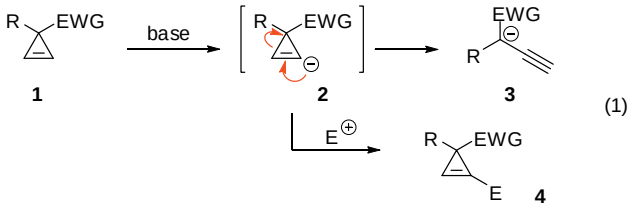
A remarkable stability of anionic species generated from cyclopropene-3-carboxamides toward ring-opening is demonstrated. The resulting cyclopropenyllithium species can be reacted with a range of electrophiles, which allows for efficient introduction of additional substituents at C1 of the strained ring.



## 1. Introduction

Cyclopropene-3-carboxamides and closely related *N*-acyl derivatives are attractive pharmacophores[1] and practical versatile synthons,[2,3] which have lately become a focus of attention, primarily owing to the increasing interest in highly selective transformations of cyclopropenes.[4] The most recent advancements in this area include the employment of optically active cyclopropene-3-carboxamides and related imides in diastereoselective addition reactions;[5] synthesis of enantiomerically enriched cyclopropenes via the diastereomeric chromatographic separation,[6] parallel kinetic resolution,[7] and enantioselective desymmetrization.[8] It was also demonstrated that certain sterically hindered imide substituents can significantly stabilize the structure of otherwise very fragile mono-substituted cyclopropenes.[9] Our group has recently demonstrated that the amide function at C3 of cyclopropene can be used to efficiently control the facial selectivity in additions of O–H and P–H entities to the cyclopropene double bond.[10] A practical synthetic approach to cyclopropene-3-carboxamides was also disclosed,[11] which allowed for efficient and scalable synthesis of these substrates. However, this methodology is limited to preparation of 1,2-unsubstituted cyclopropenes only. Accordingly, we sought complementary synthetic methods to further expand the scope of available cyclopropenylcarboxamides.

Due to relatively high acidity of the C($sp^2$)–H bonds in cyclopropenes, their deprotonation usually proceeds routinely providing a convenient tool for further functionalization of the double bond. However, electron-withdrawing substituents at C-3 are well known to promote facile ring-opening and rearrangement into a thermodynamically more stable propargyl anion **3** (Eq. 1).[12] Several approaches have been developed to circumvent this unwanted process. Thus, Eckert-Maksic demonstrated that cyclic anion **2**, generated from cyclopropene **1** by slow addition of a non-nucleophilic base, can be efficiently intercepted with silyl- or germyl-chlorides.[13] This strategy was also employed by Fox[14] and Gevorgyan[15] to install a silyl protection at the double bond of cyclopropene-3-carboxylates.




(1)

This protocol, however, cannot be used for selective installation of a single silyl group at the double bond of 1,2-unsubstituted cyclopropenes, and is inapplicable to reactions with carbon-based electrophiles. Recently, Fox disclosed a useful method for generation of a dianionic carboxylate species **2** (EWG=$CO_2^-$), which permitted efficient trapping of the cyclopropenyl anion with a wide range of electrophiles.[16] This dianionic species, however, required the presence of a stabilizing additive, an amine *N*-oxide, for efficient coupling with certain less reactive electrophiles.[16b] Alternative methods for ring-retentive derivatization of cyclopropene-3-carboxylic acids include Pd-catalyzed electrophilic arylation[17] and Morita–Baylis–Hillman reaction[15] reported by Gevorgyan, as well as Lam's Cu-catalyzed silylation[18] and fluoride-assisted stannylation[19] reactions. Herein, we demonstrate an efficient and chemoselective method for synthesis of trisubstituted cyclopropene-3-carboxamides (**4**, EWG=$CONR_2$) via a ring-retentive deprotonation of cyclopropene-3-carboxamides (**1**), followed by trapping of the cyclopropenylmetal species with electrophilic reagents.

* Corresponding author. Tel.: +1 785 864 5071; fax: +1 785 864 5396; e-mail address: mrubin@ku.edu (M. Rubin).

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doi:10.1016/j.tet.2010.04.123

## 2. Results and discussion

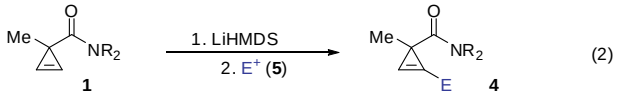
The reasoning behind our trial experiments was the anticipated increased stability of our cyclopropenylcarboxamide anions, bearing a relatively electron-rich amide function, toward ring-opening. Analogously to the cyclopropenylcarboxylate dianions, which were successfully employed in ring-retentive deprotonation,[16] the amide group was expected to impart additional stabilization to the strained anionic species. Accordingly, we exposed *N*,*N*-diethyl-1-methylcycloprop-2-enecarboxamide (**1a**) to a range of different bases, while trapping the resulting cyclopropenyllithium species with a suitable electrophile (Table 1). The initial experiments involving quenching reaction mixtures with methyl iodide were discouraging, providing complex mixtures containing both cyclopropenes and ring-opening products. In contrast, deprotonation of **1a** followed by trapping with dimethyl sulfate (**5a**) occurred with retention of the three-membered ring, affording inseparable mixtures of mono- (**4aa**) and dimethylation (**6a**) products.

**Table 1**
Optimization of the ring-retentive lithiation[a]

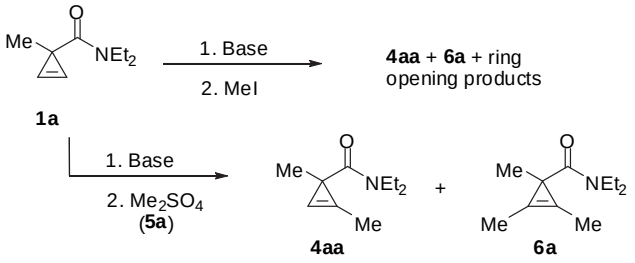
| # | Base | Electrophile (equiv) | **1a**/**4aa**/**6a**[b] |
|---|---|---|---|
| 1 | MeLi | MeI (1.05) | 20:43:14 |
| 2 | MeLi+NMO | MeI (1.05) | 17:52:16 |
| 3 | *n*-BuLi | MeI (1.05) | 20:37:11 |
| 4 | *t*-BuLi | MeI (1.05) | 18:39:12 |
| 5 | LDA | MeI (1.05) | 40:12:15 |
| 6 | LiHDMS | MeI (1.05) | 15:18:14 |
| 7 | MeLi | DMS (1.05) | 31:59:9 |
| 8 | MeLi+NMO | DMS (1.05) | 14:72:12 |
| 9 | *n*-BuLi | DMS (1.05) | 32:60:10 |
| 10 | *t*-BuLi | DMS (1.05) | 29:57:11 |
| 11 | LDA | DMS (1.05) | 50:17:13 |
| *12* | *LiHDMS* | *DMS (1.05)* | *15:75:5* |
| *13* | *LiHDMS*[c] | *DMS (3.00)* | *0:12:82* |

[a] All reactions shown in this table were performed at −30 °C in THF.
[b] GC yields are provided, obtained from quantitative analysis employing *n*-octane as internal standard. The rest of material balance should account for unidentified ring-opening products.
[c] Base (3.00 equiv) was used.

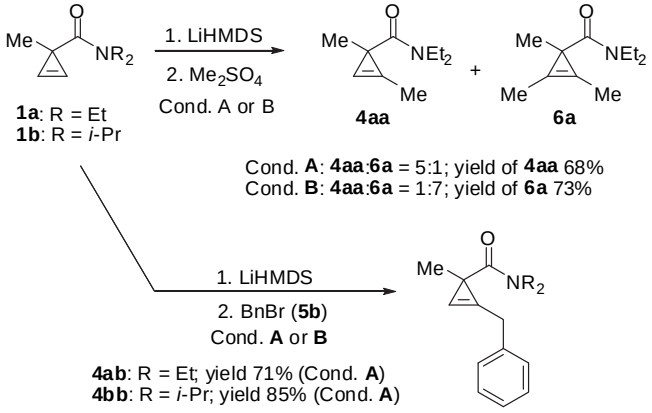
After substantial optimization (Table 1), it was found that selective mono-deprotonation can be carried out in the presence of 1.5 equiv of LiHMDS[20] in THF at −30 °C. Upon addition of 1.05 equiv dimethyl sulfate to the resulting anion, the corresponding trisubstituted cyclopropene **4aa** was obtained as a major product in good yield (Scheme 2, Conditions A). Employment of excess base and electrophile allowed for predominant formation of bis-methylated product **6a** (Scheme 2, Conditions B). Remarkably, no stabilizing additives were necessary to preserve the strained cyclic anion. Next, we tested other electrophiles in the reaction with cyclopropenyl species generated under conditions A. Thus, reaction of **1a** with benzyl bromide (**5b**) afforded trisubstituted cyclopropene **4ab** as a sole product in high isolated yield (Scheme 2). The analogous reaction of a more sterically hindered diisopropyl amide **1b** also proceeded uneventfully, providing product **4bb** in excellent yield. Interestingly, in contrast to the methylation reaction described above, all our attempts to effect double alkylation of **1a**,**b** with benzyl bromide failed, providing only monobenzylated products **4ab** and **4bb**, respectively. Remarkably, under these very mild reaction conditions no base assisted migration of the strained double bond into exocyclic position was observed. We rationalized that the bulky base employed in this transformation makes deprotonation at the benzylic position inefficient under our reaction conditions. In striking contrast to the above examples (Scheme 2), treatment of the cyclopropenyl anions **2c** and **2d** with equimolar amounts of allyl iodide afforded dienynes **7c**,**d** as the only isolable products in low yield (Scheme 4). When we doubled the amount of both base and allyl iodide, compounds **7c** and **7d** were obtained in good yields as sole products. It should be mentioned that complementary experiments involving the quenching of **2c**,**d** with a proton source returned unchanged starting materials, indicating the electrophile plays a crucial role in the observed ring-opening (Scheme 4). We speculated that the Lewis acidity of lithium iodide



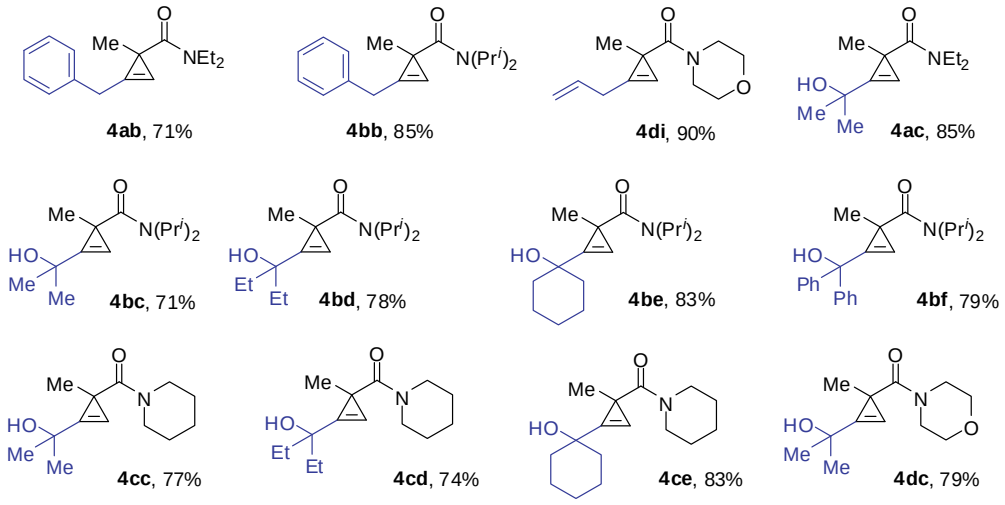

produced in this reaction, as well as in the reaction with MeI described above (Scheme 1), promotes cleavage of the three-membered ring.[21] To obtain experimental evidences in support of this idea we examined electrophilic trapping of the cyclopropenyllithium species generated from cyclopropene **1d** in the presence of allyl bromide (**5i**). Remarkably, no ring cleavage was observed in this case, and 1-allylcyclopropene **4di** was obtained in high yield (Scheme 5), suggesting that the much less Lewis acidic lithium bromide byproduct does not cause the ring cleavage under the reported conditions. Similarly to the electrophilic benzylation demonstrated above, no migration of the cyclopropene double bond into the exocyclic position took place in the allylated product. At the same time, carrying out the same reaction in the presence of 1.5 equiv of lithium iodide enabled ring cleavage to give **7c** as the only isolable product. It should be mentioned that non-activated electrophiles, such as *n*-butylbromide, did not react with cyclopropenyllithium species **2c**, and lead to recovery of the starting material **1c**.



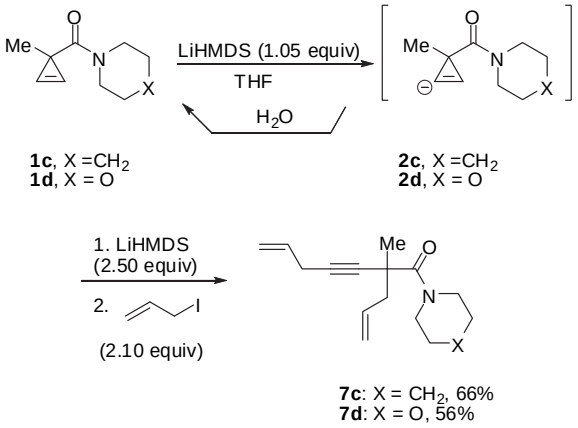

**Scheme 1.** Base: MeLi, *n*-BuLi, MeLi+NMO, *t*-BuLi, LDA, LiHMDS.



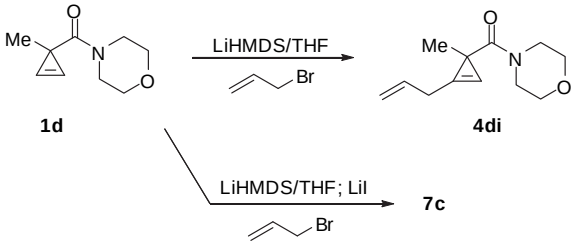

**Scheme 2.** Conditions A: LiHMDS (1.50 equiv; electrophile 1.05 equiv). Conditions B: LiHMDS (3.00 equiv; electrophile 2.10 equiv).




**Scheme 3.** Synthesis of trisubstituted cyclopropenes via ring-retentive mono-deprotonation of cyclopropene-3-carboxamides.



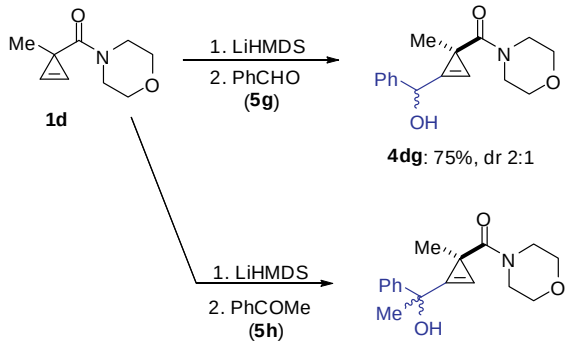

**Scheme 4.** Ring-opening of cyclopropenyl anion upon electrophilic trapping with allyl iodide.




**Scheme 5.**

Next, a series of carbonyl electrophiles were examined in order to access cyclopropenylcarbinols, which are useful synthons for organic chemistry.[22] The reactions proceeded smoothly with benzaldehyde and acetophenone, providing inseparable mixtures of diastereomeric mono-adducts **4dg** and **4dh** (Scheme 6). Symmetric aliphatic ketones **5c**–**e** reacted effortlessly at −30 °C, providing the corresponding strained allylic alcohols **4ac**, **4bc**, **4bd**, **4be**, **4cc**, **4cd**, **4ce**, and **4dc** in high yields (Scheme 3). Reaction of **1b** with bulky benzophenone (**5f**) to afford **4bf** required prolonged heating at 65 °C to achieve complete conversion (Scheme 3). Nonetheless, even under such harsh condition, no ring-opening products were detected.

In conclusion, it was demonstrated that anionic species generated from cyclopropene-3-carboxamides possess remarkable stability toward ring-opening, even at elevated temperatures, without employment of stabilizing additives. This feature sets them apart from all the previously described carbonyl derivatives of cyclopropenes. The resulting cyclopropenyllithium species can be reacted with a range of electrophiles, which allows for efficient introduction of additional substituents at C1 of the strained ring.




**Scheme 6.**

Unusual reactivity of allyl iodide in the electrophilic trapping of cyclopropenyllithium species was observed, which resulted in a rapid ring-opening promoted by lithium iodide, affording (diallylpropargyl)carboxamides.

## 3. Experimental part

### 3.1. General

NMR spectra were recorded on a Bruker Avance DPX-400 instrument, equipped with a quadruple-band gradient probe (H/C/P/F QNP) or a Bruker Avance DRX-500 with a dual carbon/proton

cryoprobe (CPDUL). The abbreviation 'app. t' is used to describe apparent triplets (i.e., double doublets with unresolved central line, or unresolved higher order multiplets in a shape of a triplet) in $^1$H NMR spectra. $^{13}$C NMR spectra were registered with broad-band 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. GC analyses were performed on a Shimadzu GC-2010 gas chromatograph with FID detector and equipped with an AOC-20i auto-injector and an AOC-20S auto-sampler tray (150 vials); 30 m×0.25 mm×0.25 μm capillary column, SHR5XLB, polydimethylsiloxane; 5% Ph was employed. Helium (99.96%), additionally purified by passing consecutively through a CRS oxygen/ moisture/hydrocarbon trap (#202839) and VICI oxygen/ moisture trap (P100-1), was used as a carrier gas. Carrier gas flow rate (1 mL/min) was stabilized using constant linear velocity algorithm. Hydrogen gas was used as FID fuel; zero-grade air and zero-grade nitrogen were used as an oxidant and make-up gas, respectively, for the FID. All these gases were purified by passing through CRS #202839 traps. The following GC parameters were used for all analyses: carrier gas flow rate 0.68 mL/min with constant linear velocity 29.9 sm/s; oven temperature program: 50 °C (2 min)−20 °C/min−275 °C (6 min), injector temperature 275 °C. Glassware employed in moisture-free syntheses was flame-dried in vacuum prior to use. A combination of glovebox and standard Schlenk technique was used to handle moisture sensitive materials. Column chromatography was carried out on silica gel (Selecto Scientific, 63–200 μm). Pre-coated silica gel plates (Merck Kiezelgel 60 F-254) were used for TLC analyses. Anhydrous tetrahydrofuran was obtained by passing degassed commercially available stabilizer-free solvent consecutively through two columns filled with activated alumina (Innovative Technology). Cyclopropenes **1a**–**d** were obtained according to the procedure, described in our recent report.[20] All other reagents were purchased from Sigma–Aldrich, Alpha-Aesar or Acros Organics and used as received.

### 3.2. 2-Benzyl-*N*,*N*-diethyl-1-methylcycloprop-2-enecarboxamide (4ab)

Typical procedure: An oven dried 25 mL round-bottomed flask was charged with lithium hexamethyldisilazide (400 mg, 2.39 mmol, 1.50 equiv) and anhydrous THF (5 mL). The mixture was stirred at −30 °C, and cold solution of cyclopropene **1a** (244 mg, 1.59 mmol, 1.00 equiv) in dry THF (5 mL) was added via cannula to obtain bright orange-red solution. The mixture was stirred for 5 min at −30 °C before benzyl bromide (200 μL, 286 mg, 1.67 mmol, 1.05 equiv) was added via syringe. Then the mixture was stirred for 2 h at −30 °C, when GC showed the reaction complete. Brine (20 mL) and ethyl acetate (20 mL) were added, organic layer was separated, and aqueous phase was extracted with ethyl acetate (2×10 mL). Combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuum. Preparative column chromatography on Silica gel (eluent hexanes/EtOAc, 2:1) afforded yellow viscous oil, $R_f$ 0.25, yield 285 mg (1.13 mmol, 71%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 7.54 (d, $J$=7.9 Hz, 2H), 7.35 (app. t, $J$=7.9 Hz, 2H), 7.25 (t, $J$=7.9 Hz, 1H), 6.82 (app. t, $J$=2.2 Hz, 1H), 3.67 (br, 2H), 3.43 (br, 1H), 3.35 (br, 1H), 2.06 (dd, $J$=9.5, 2.2 Hz, 1H), 1.50 (s, 3H), 1.49 (dd, $J$=9.5, 2.2 Hz, 1H), 1.29 (br, 3H), 1.14 (br, 3H); $^{13}$C NMR (125.76 MHz, $CDCl_3$) $\delta$ 170.6, 137.3, 129.7, 128.5 (+, 2C), 127.3 (+), 126.8 (+, 2C), 118.0 (+), 41.5 (−), 39.1 (−), 23.2, 22.0 (+), 17.1 (−), 14.1 (+), 12.6 (+); IR (film, cm$^{-1}$): 2972, 2934, 2873, 1780, 1720, 1634, 1454, 1427, 1381, 1221, 1157, 748, 696, 505; GC: $t_R$ 11.75 min; HRMS (TOF ES): found 244.1700, calculated for $C_{16}H_{22}NO$ (M+H) 244.1701 (0.4 ppm).

### 3.3. *N*,*N*-Diethyl-1,2-dimethylcycloprop-2-enecarboxamide (4aa)

The reaction was performed according to a typical procedure, employing cyclopropene **1a** (274 mg, 1.64 mmol) and dimethyl sulfate (163 μL, 217 mg, 1.72 mmol) as an electrophile to afford the title compound as colorless oil, $R_f$ 0.49 ($CH_2Cl_2$/THF, 5:1). Yield 187 mg (1.12 mmol, 68%); $^1$H NMR (400.13 MHz, $CDCl_3$) $\delta$ 6.67 (s, 1H), 3.57–3.27 (br m, 4H), 2.18 (s, 3H), 1.26 (s, 3H), 1.22–1.15 (br m, 3H), 1.14–1.06 (br m, 3H); $^{13}$C NMR (100.67 MHz, CDCl3) $\delta$ 176.2, 123.6, 105.2 (+), 41.3 (br, −), 38.3 (br, −), 24.8, 22.3 (+), 14.3 (br, +), 12.6 (br, +), 9.8 (+); IR (film, cm$^{-1}$): 2968, 2933, 2920, 2872, 1772, 1624, 1458, 1421, 1379, 1364, 1281, 1207, 1151, 1101, 845, 795, 764, 750, 694; HRMS (TOF ES): found 166.1234, calculated for $C_{10}H_{16}NO$ (M−H) 166.1232 (1.2 ppm).

### 3.4. *N*,*N*-Diethyl-1,2,3-trimethylcycloprop-2-enecarboxamide (6a)

The reaction was performed according to a typical procedure, employing cyclopropene **1a** (274 mg, 1.64 mmol), lithium hexamethyldisilazide (823 mg, 492 mmol, 3.00 equiv), and dimethyl sulfate (467 μL, 620 mg, 4.92 mmol) as an electrophile to afford the title compound as colorless oil, $R_f$ 0.56 ($CH_2Cl_2$/THF, 5:1). Yield 217 mg (1.20 mmol, 73%); $^1$H NMR (400.13 MHz, $CDCl_3$) $\delta$ 3.52 (br s, 2H), 3.33 (br s, 2H), 2.06 (s, 6H), 1.27 (br s, 3H), 1.20 (s, 3H), 1.11 (br s, 3H); $^{13}$C NMR (100.67 MHz, $CDCl_3$) $\delta$ 177.2, 112.5 (2C), 41.3 (br, −), 38.1 (br, −), 26.0, 20.3 (+), 14.4 (br, +), 12.9 (br, +), 8.6 (+, 2C); IR (film, cm$^{-1}$): 2968, 2918, 1626, 1460, 1435, 1421, 1379, 1362, 1279, 1209, 1151, 1101, 793, 750, 638; HRMS (TOF ES): found 181.1466, calculated for $C_{11}H_{19}NO$ ($M^+$) 181.1467 (0.6 ppm).

### 3.5. 2-Benzyl-*N*,*N*-diisopropyl-1-methylcycloprop-2-enecarboxamide (4bb)

The reaction was performed according to a typical procedure, employing cyclopropene **1b** (296 mg, 1.64 mmol) and benzyl bromide (206 μL, 295 mg, 1.72 mmol) as an electrophile to afford the title compound as yellow viscous oil, $R_f$ 0.25 (hexanes/EtOAc, 2:1). Yield 376 mg (1.39 mmol, 85%); $^1$H NMR (400.13 MHz, $CDCl_3$) $\delta$ 7.54 (d, $J$=7.1 Hz, 2H), 7.35 (app. t, $J$=7.3 Hz, 2H), 7.25 (app. t, $J$=7.3 Hz, 1H), 6.77 (t, $J$=2.3 Hz, 1H), 4.53 (br septet, $J$=5.8 Hz, 1H), 3.35 (br septet, $J$=6.3 Hz, 1H), 2.05 (dd, $J$=9.9, 2.3 Hz, 1H), 1.48 (s, 3H), 1.44 (dd, $J$=9.9, 2.3 Hz, 1H), 1.42 (d, $J$=5.8 Hz, 3H), 1.37 (d, $J$=6.3 Hz, 3H), 1.33 (d, $J$=5.8 Hz, 3H), 1.27 (d, $J$=6.3 Hz, 3H); $^{13}$C NMR (100.67 MHz, $CDCl_3$) $\delta$ 170.0, 137.3, 129.8, 128.5 (+, 2C), 127.2 (+), 126.7 (+, 2C), 117.4 (+), 48.9 (+), 45.8 (+), 24.3, 21.7 (+), 21.0 (+), 20.7 (+), 20.5 (+), 20.2 (+), 17.0 (−); IR (film, cm$^{-1}$): 2999, 2966, 2930, 2870, 1636, 1452, 1435, 1367, 1329, 1211, 1153, 1040, 746, 694, 509; GC: $t_R$ 12.06 min; HRMS (TOF ES): found 278.2099, calculated for $C_{18}H_{25}NOLi$ (M+Li) 278.2096 (1.1 ppm).

### 3.6. *N*,*N*-Diethyl-2-(2-hydroxypropan-2-yl)-1-methylcycloprop-2-enecarboxamide (4ac)

The reaction was performed according to a typical procedure, employing cyclopropene **1a** (274 mg, 1.64 mmol) and acetone (126 μL, 100 mg, 1.72 mmol) as an electrophile to afford the title compound as colorless viscous oil, $R_f$ 0.24 (hexanes/EtOAc, 5:1). Yield 376 mg (1.39 mmol, 85%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 6.50 (s, 1H), 5.74 (br s, 1H), 3.50 (q, $J$=7.3 Hz, 2H), 3.36 (dq, $J$=14.2, 7.3 Hz, 1H), 3.12 (dq, $J$=14.2, 7.3 Hz, 1H), 1.45 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 1.15 (t, $J$=7.3 Hz, 3H), 1.03 (s, $J$=7.3 Hz, 3H); $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 176.2, 133.0, 101.8 (+), 66.9, 42.1 (−), 38.8 (−), 29.1 (+), 28.8 (+), 27.9, 22.5 (+), 14.2 (+), 12.5 (+); IR (film, cm$^{-1}$): 3329 (br), 3105, 2974, 2934, 2876, 1765, 1703, 1599, 1462,

1429, 1377, 1362, 1315, 1285, 1219, 1169, 1105, 945, 683, 608, 538; GC: $t_R$ 8.70 min; HRMS (TOF ES): found 212.1650, calculated for $C_{12}H_{22}NO$ (M+H) 212.1651 (0.4 ppm).

### 3.7. 2-(2-Hydroxypropan-2-yl)-*N*,*N*-diisopropyl-1-methylcycloprop-2-enecarboxamide (4bc)

The reaction was performed according to a typical procedure, employing cyclopropene **1b** (296 mg, 1.64 mmol) and acetone (126 μL, 100 mg, 1.72 mmol) as an electrophile to afford the title compound as colorless solid, mp 78–79 °C, $R_f$ 0.17 (hexanes/EtOAc, 5:1). Yield 278 mg (1.16 mmol, 71%); $^1$H NMR (400.13 MHz, $CDCl_3$) $\delta$ 6.55 (s, 1H), 6.01 (br s, 1H), 4.48 (septet, $J$=6.8 Hz, 1H), 3.30 (septet, $J$=6.8 Hz, 1H), 1.54 (s, 3H), 1.48 (s, 3H), 1.40 (d, $J$=6.8 Hz, 3H), 1.39 (s, 3H), 1.35 (d, $J$=6.8 Hz, 3H), 1.28 (d, $J$=6.8 Hz, 3H), 1.19 (d, $J$=6.8 Hz, 3H); $^{13}$C NMR (100.67 MHz, $CDCl_3$) $\delta$ 176.1, 134.1, 101.6 (+), 66.8, 49.9 (+), 45.4 (+), 29.4, 29.2 (+), 28.8 (+), 22.4 (+), 21.0 (+), 20.6 (+), 20.4 (+), 20.2 (+); IR (film, cm$^{-1}$): 3250 (br), 3119, 2966, 2923, 1763, 1589, 1537, 1473, 1458, 1429, 1373, 1340, 1209, 1153, 1040, 970, 951, 895, 735, 671, 608; GC: $t_R$ 9.10 min; HRMS (TOF ES): found 239.1876, calculated for $C_{14}H_{25}NO_2$ ($M^+$) 239.1885 (3.8 ppm).

### 3.8. 2-(3-Hydroxypentan-3-yl)-*N*,*N*-diisopropyl-1-methylcycloprop-2-enecarboxamide (4bd)

The reaction was performed according to a typical procedure, employing cyclopropene **1b** (303 mg, 1.68 mmol) and diethyl ketone (186 μL, 152 mg, 1.76 mmol) as an electrophile to afford the title compound as yellowish viscous oil, $R_f$ 0.35 (hexanes/EtOAc, 4:1). Yield 349 mg (1.31 mmol, 78%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 6.60 (s, 1H), 5.98 (br s, 1H), 4.47 (septet, $J$=6.6 Hz, 1H), 3.27 (septet, $J$=6.6 Hz, 1H), 1.79–1.64 (m, 4H), 1.38 (d, $J$=6.6 Hz, 3H), 1.35 (s, 3H), 1.32 (d, $J$=6.6 Hz, 1H), 1.26 (d, $J$=6.9 Hz, 1H), 1.16 (d, $J$=6.9 Hz, 1H), 0.92–0.88 (m, 6H); $^{13}$C NMR (100.67 MHz, $CDCl_3$) $\delta$ 175.9, 133.1, 103.7 (+), 73.2, 49.7 (+), 45.2 (+), 32.1 (−), 32.0 (−), 28.2, 22.4 (+), 20.9 (+), 20.5 (+), 20.1 (+), 20.0 (+), 8.5 (+), 7.9 (+); IR (film, cm$^{-1}$): 3269 (br), 3103, 3001, 2966, 2935, 2878, 1759, 1597, 1537, 1443, 1370, 1339, 1213, 1153, 1138, 1105, 1038, 968, 943, 901, 833, 769, 721, 658, 604, 555, 530, 511, 492; GC: $t_R$ 10.35 min; HRMS (TOF ES): found 267.2200, calculated for $C_{16}H_{29}NO_2$ ($M^+$) 267.2198 (0.7 ppm).

### 3.9. 2-(1-Hydroxycyclohexyl)-*N*,*N*-diisopropyl-1-methylcycloprop-2-enecarboxamide (4be)

The reaction was performed according to a typical procedure, employing cyclopropene **1b** (286 mg, 1.59 mmol) and cyclohexanone (173 μL, 164 mg, 1.67 mmol) as an electrophile to afford a title compound as yellowish solid, mp 52–53 °C, $R_f$ 0.32 (hexanes/EtOAc, 5:1). Yield 368 mg (1.32 mmol, 83%); $^1$H NMR (400.13 MHz, $CDCl_3$) $\delta$ 6.65 (s, 1H), 6.21 (br s, 1H), 4.48 (septet, $J$=6.6 Hz, 1H), 3.29 (septet, $J$=6.8 Hz, 1H), 1.97–1.88 (m, 2H), 1.82–1.64 (m, 5H), 1.54–1.44 (m, 3H), 1.39 (d, $J$=6.8 Hz, 3H), 1.37 (s, 3H), 1.34 (d, $J$=6.8 Hz, 3H), 1.27 (d, $J$=6.6 Hz, 3H), 1.17 (d, $J$=6.6 Hz, 3H); $^{13}$C NMR (100.67 MHz, $CDCl_3$) $\delta$ 176.1, 132.8, 103.6 (+), 69.4, 49.8 (+), 45.4 (+), 38.5 (−), 37.8 (−), 28.1, 25.5 (−), 23.30 (−), 23.27 (−), 22.4 (+), 21.0 (+), 20.6 (+), 20.4 (+), 20.2 (+); IR (film, cm$^{-1}$): 3285 (br), 3001, 2964, 2932, 2856, 1599, 1443, 1369, 1337, 1211, 1155, 1038, 968, 600, 507; GC: $t_R$ 11.50 min; HRMS (TOF ES): found 279.2193, calculated for $C_{17}H_{29}NO_2$ ($M^+$) 279.2198 (1.8 ppm).

### 3.10. 2-(Hydroxydiphenylmethyl)-*N*,*N*-diisopropyl-1-methylcycloprop-2-enecarboxamide (4bf)

The reaction was performed according to a typical procedure, employing cyclopropene **1b** (292 mg, 1.62 mmol) and benzophenone (310 mg, 1.70 mmol) as an electrophile (after addition of benzophenone the reaction mixture was heated to 65 °C overnight to force the complete conversion) to afford the title compound as colorless solid, mp 140–142 °C, $R_f$ 0.17 (hexanes/EtOAc, 5:1). Yield 465 mg (1.28 mmol, 79%); $^1$H NMR (400.13 MHz, $CDCl_3$) $\delta$ 7.64–7.58 (m, 2H), 7.36–7.21 (m, 8H), 6.91 (s, 1H), 4.47 (septet, $J$=6.6 Hz, 1H), 3.31 (septet, $J$=6.6 Hz, 1H), 1.60 (br s, 1H), 1.41 (d, $J$=6.6 Hz, 3H), 1.35 (d, $J$=6.6 Hz, 3H), 1.27 (d, $J$=6.6 Hz, 3H), 1.19 (d, $J$=6.6 Hz, 3H), 1.13 (s, 3H); $^{13}$C NMR (100.67 MHz, $CDCl_3$) $\delta$ 175.8, 146.3, 144.7, 132.9, 128.0 (+, 2C), 127.9 (+), 127.1 (+), 126.9 (+, 2C), 126.5 (+, 2C), 126.2 (+, 2C), 104.9 (+), 74.7, 50.0 (+), 45.6 (+), 30.2, 21.2 (+), 21.0 (+), 20.6 (+), 20.3 (+), 20.2 (+); IR (film, cm$^{-1}$): 3339 (br), 3032, 3001, 2966, 2932, 2872, 1759, 1591, 1447, 1369, 1340, 1207, 1151, 1036, 1018, 750, 698, 638, 615, 577, 554, 505; GC: $t_R$ 14.50 min; HRMS (TOF ES): found 363.2205, calculated for $C_{24}H_{29}NO_2$ ($M^+$) 363.2198 (1.9 ppm).

### 3.11. 2-[3-Methyl-3-(piperidin-1-ylcarbonyl)cycloprop-1-en-1-yl]propan-2-ol (4cc)

The reaction was performed according to a typical procedure, employing cyclopropene **1c** (249 mg, 1.51 mmol) and acetone (117 μL, 92 mg, 1.59 mmol) as an electrophile to afford the title compound as colorless viscous oil, $R_f$ 0.16 (hexanes/EtOAc, 3:1). Yield 259 mg (1.16 mmol, 77%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 6.58 (s, 1H), 5.79 (br s, 1H), 3.71–3.42 (m, 4H), 1.70–1.53 (m, 6H), 1.54 (s, 3H), 1.47 (s, 3H), 1.41 (s, 3H); $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 175.3, 132.9, 101.9 (+), 67.0, 47.3 (−), 42.8 (−), 29.1 (+), 28.9 (+), 27.6, 26.6 (−), 25.4 (−), 24.4 (−), 22.5 (+); IR (film, cm$^{-1}$): 3317 (br), 3101; 2974, 2935, 2856, 1765, 1601, 1531, 1443, 1373, 1358, 1271, 1259, 1240, 1224, 1165, 1115, 1011, 972, 953, 854, 727, 688, 608, 528, 416; GC: $t_R$ 10.26 min; HRMS (TOF ES): found 206.1540, calculated for $C_{13}H_{20}NO$ (M−OH) 206.1545 (2.4 ppm).

### 3.12. 3-[3-Methyl-3-(piperidin-1-ylcarbonyl)cycloprop-1-en-1-yl]pentan-3-ol (4cd)

The reaction was performed according to a typical procedure, employing cyclopropene **1c** (249 mg, 1.51 mmol) and diethyl ketone (168 μL, 137 mg, 1.59 mmol) as an electrophile to afford a title compound as yellowish viscous oil, $R_f$ 0.28 (hexanes/EtOAc, 2:1). Yield 262 mg (1.12 mmol, 74%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 6.64 (s, 1H), 5.76 (br s, 1H), 3.70–3.40 (m, 4H), 1.81–1.68 (m, 4H), 1.68–1.50 (m, 6H), 1.38 (s, 3H), 0.94 (t, $J$=7.6 Hz, 3H), 0.92 (t, $J$=7.6 Hz, 3H); $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 175.3, 131.8, 103.8 (+), 73.3, 47.3 (−), 42.8 (−), 31.99 (−), 31.96 (−), 26.58, 26.54 (−), 25.4 (−), 24.4 (−), 22.7 (+), 8.6 (+), 8.1 (+); IR (film, cm$^{-1}$): 3308 (br), 3097, 2966, 2937, 2858, 1715, 1601, 1529, 1443, 1373, 1271, 1259, 1240, 1155, 1115, 1011, 968, 874, 852, 723, 687, 602, 530; GC: $t_R$ 11.45 min; HRMS (TOF ES): found 252.1967, calculated for $C_{15}H_{26}NO_2$ (M+H) 252.1963 (1.6 ppm).

### 3.13. 1-[3-Methyl-3-(piperidin-1-ylcarbonyl)cycloprop-1-en-1-yl]cyclohexanol (4ce)

The reaction was performed according to a typical procedure, employing cyclopropene **1c** (249 mg, 1.51 mmol) and cyclohexanone (164 μL, 156 mg, 1.59 mmol) as an electrophile to afford the title compound as colorless viscous oil, $R_f$ 0.27 (hexanes/EtOAc, 3:1). Yield 330 mg (1.25 mmol, 83%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 6.68 (s, 1H), 5.96 (br s, 1H), 3.72–3.41 (m, 4H), 1.98–1.92 (m, 1H), 1.82–1.62 (m, 8H), 1.60–1.45 (m, 5H), 1.40 (s, 3H), 1.35–1.26 (m, 3H); $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 175.4, 131.7, 103.9 (+), 69.7, 47.3 (−), 42.8 (−), 38.6 (−), 37.8 (−), 26.6 (−), 26.3, 25.43 (−), 25.36 (−), 24.4 (−), 23.30 (−), 23.27 (−), 22.5 (+); IR (film, cm$^{-1}$): 3300 (br), 3097, 2932, 2854, 1763, 1601, 1528, 1445, 1371, 1348, 1273, 1157, 1115, 1078, 1030, 1011, 968, 905, 852, 725, 685, 598, 529; GC: $t_R$

11.75 min; HRMS (TOF ES): found 264.1963, calculated for $C_{16}H_{26}NO_2$ (M+H) 264.1963 (0.0 ppm).

### 3.14. 2-[3-Methyl-3-(morpholin-4-ylcarbonyl)cycloprop-1-en-1-yl]propan-2-ol (4dc)

The reaction was performed according to a typical procedure, employing cyclopropene **1d** (167 mg, 1.00 mmol) and acetone (77 μL, 61 mg, 1.05 mmol) as an electrophile to afford the title compound as colorless viscous oil, $R_f$ 0.34 (hexanes/EtOAc 1:5). Yield 179 mg (0.79 mmol, 79%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 6.59 (s, 1H), 5.39 (s, 1H), 3.77–3.45 (br m, 8H), 1.54 (s, 3H), 1.47 (s, 3H), 1.41 (s, 3H); $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 175.7, 132.6, 101.8 (+), 67.2, 66.79 (br s., –, 2C), 46.8 (br s., –), 42.2 (br s., –), 29.1 (+), 28.9 (+), 27.2, 22.3 (+); IR (film, cm$^{-1}$): 3024 (br), 2974, 2926, 2860, 1601, 1462, 1434, 1213, 1153, 1113, 1030, 839; GC: $t_R$ 10.47 min; HRMS (TOF ES): found 225.1368, calculated for $C_{12}H_{19}NO_3$ ($M^+$) 225.1365 (1.3 ppm).

### 3.15. [3-Methyl-3-(morpholin-4-ylcarbonyl)cycloprop-1-en-1-yl](phenyl)methanol (4dg)

The reaction was performed according to a typical procedure, employing cyclopropene **1d** (150 mg, 0.90 mmol) and freshly distilled benzaldehyde (203 μL, 212 mg, 2 mmol) as an electrophile to afford the title compound as light-yellow viscous oil, $R_f$ 0.42 ($CH_2Cl_2$/EtOAc, 3:2). Yield 184 mg (0.67 mmol, 75%), dr 2:1; $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 7.57–7.74 (m, 2H), 7.39–7.74 (m, 2H), 7.32–7.27 (m, 1H), [6.75 (s) and 6.68 (s), Σ1H], 6.07 (br s, 1H), [5.88 (s) and 5.68 (s), Σ1H], 3.75–3.50 (m, 8H), [1.39 (s) and 1.13 (s), Σ3H]; $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 175.6, 175.5, 142.0, 140.9, 129.7, 129.5, 128.4 (+), 127.7 (+), 127.6 (+), 126.14 (+), 126.09 (+), 105.1 (+), 103.4 (+), 67.5 (+), 67.3 (+), 66.8 (–, br), 46.8 (–), 46.5 (–), 42.6 (–), 42.3 (–), 27.6, 27.1, 21.6 (+), 21.5 (+); IR (film, cm$^{-1}$): 3303 (br), 3061, 2964, 2922, 2856, 1632, 1493, 1275, 1256, 1213, 1153, 1115, 1030, 700; HRMS (TOF ES): found 274.1441, calculated for $C_{16}H_{20}NO_3$ (M+H) 274.1443 (0.7 ppm).

### 3.16. [2-(1-Hydroxy-1-phenylethyl)-1-methylcycloprop-2-en-1-yl](morpholin-4-yl)methanone (4dh)

The reaction was performed according to a typical procedure, employing cyclopropene **1d** (150 mg, 0.90 mmol) and acetophenone (233 μL, 240 mg, 2 mmol) as an electrophile to afford a title compounds as light-yellow viscous oil, $R_f$ 0.29 (hexanes/EtOAc, 1:2). Yield 161 mg (0.56 mmol, 62%), dr 1:1; $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 7.63–7.58 (m, 2H), 7.39–7.33 (m, 2H), 7.29–7.25 (m, 1H), [6.77 (s) and 6.64 (s), Σ1H], [6.30 (br s) and 6.23 (br s), Σ1H], 3.75–3.50 (m, 8H), [1.86 (s) and 1.78 (s), Σ3H], [1.53 (s) and 1.00 (s), Σ3H]; $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 175.6, 175.4, 146.4, 145.1, 132.5, 132.0, 128.1 (+, 2C), 128.0 (+, 2C), 127.0 (+), 126.9 (+), 125.2 (+, 2C), 124.8 (+, 2C), 103.3 (+), 102.4 (+), 71.0, 70.5, 66.7 (–, br, 4C), 46.8 (–, br, 2C), 42.2 (–, br, 2C), 30.6 (+), 29.6 (+), 28.1, 27.9, 22.3 (+), 21.0 (+); IR (film, cm$^{-1}$): 3279 (br), 3109, 2972, 2922, 2856, 1605, 1462, 1439, 1364, 1277, 1256, 1215, 1153, 1115, 1067, 1030, 768, 702, 623, 592; HRMS (TOF ES): found 287.1519, calculated for $C_{17}H_{21}NO_3$ ($M^+$) 287.1521 (0.7 ppm).

### 3.17. [1-Methyl-2-(prop-2-en-1-yl)cycloprop-2-en-1-yl](morpholin-4-yl)methanone (4di)

The reaction was performed according to a typical procedure, employing cyclopropene **4d** (100 mg, 0.60 mmol) and allyl bromide (53 μL, 76 mg, 0.63 mmol) as an electrophile to afford a title compound as yellow oil, $R_f$ 0.36 (hexanes/EtOAc 6:1). Yield 117 mg (0.56 mmol, 90%); $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ ppm 5.93 (ddt, $J$=16.9, 10.2, 6.5 Hz, 1H), 5.78 (s, 1H), 5.14 (ddt, $J$=16.9, 1.9, 1.6 Hz, 1H), 5.11 (ddt, $J$=10.2, 1.6, 1.3 Hz, 1H), 3.82–3.77 (m, 4H), 3.29 (dq, $J$=6.6, 1.3 Hz, 2H), 3.07–3.01 (m, 4H), 1.93 (s, 3H); $^{13}$C NMR (125.76 MHz, $CDCl_3$) $\delta$ ppm 176.3, 147.3, 134.1 (+), 116.5 (–), 108.9 (+), 67.2 (–, 2C), 51.1 (–, 2C), 32.7 (–), 29.9, 9.5 (+); IR (film, cm$^{-1}$): 3080, 2959, 2918, 2893, 2853, 1772, 1649, 1576, 1450, 1371, 1296, 1261, 1223, 1117, 1070, 920, 847, 804, 569; HRMS (TOF ES): found 206.1185, calculated for $C_{12}H_{16}NO_2$ (M–H) 206.1181 (1.9 ppm).

### 3.18. 2-Allyl-2-methyl-1-(piperidin-1-yl)hept-6-en-3-yn-1-one (7c)

The reaction was performed according to a typical procedure, employing cyclopropene **1c** (249 mg, 1.51 mmol), lithium hexamethyldisilazide (633 mg, 3.78 mmol, 2.50 equiv), and allyl iodide (291 μL, 533 mg, 3.17 mmol, 2.10 equiv) as an electrophile the afford a title compound as yellowish viscous oil, $R_f$ 0.33 (hexanes/EtOAc, 3:1). Yield 245 mg (1.00 mmol, 66%); $^1$H NMR (500.19 MHz, $CDCl_3$) $\delta$ 5.89 (dddd, $J$=17.7, 9.5, 8.2, 6.3 Hz, 1H), 5.79 (ddt, $J$=17.0, 10.2, 5.2 Hz, 1H), 5.27 (ddt, $J$=17.0, 1.9, 1.6 Hz, 1H), 5.12–5.11 (m, 1H), 5.10 5.06 (m, 2H), 3.86 (br s., 2H), 3.56 (br s., 2H), 2.98 (dt, $J$=5.4, 1.7 Hz, 2H), 2.61 (ddt, $J$=13.6, 6.5, 1.6 Hz, 1H), 2.39 (dd, $J$=13.7, 8.0 Hz, 1H), 1.61–1.67 (m, 2H), 1.60–1.52 (m, 4H), 1.40 (s, 3H); $^{13}$C NMR (125.67 MHz, $CDCl_3$) $\delta$ 170.1, 134.3 (+), 132.7 (+), 118.0 (–), 115.9 (–), 84.3, 81.4, 47.9 (br s, –), 44.4 (br s., –), 44.4 (–), 40.4, 25.9 (br s., –), 25.7 (+), 24.6 (–), 23.1 (–, 2C); GC: $t_R$ 10.97 min; IR (film, cm$^{-1}$): 3060, 2972, 2934, 2874, 1634, 1454, 1427, 1381, 1221, 1157, 748, 696, 638, 627, 505; HRMS (TOF ES): found 246.1855, calculated for $C_{16}H_{24}NO$ (M+H) 246.1858 (1.2 ppm).

### 3.19. 2-Allyl-2-methyl-1-morpholinohept-6-en-3-yn-1-one (7d)

The reaction was performed according to a typical procedure, employing cyclopropene **1d** (179 mg, 1.07 mmol), lithium hexamethyldisilazide (449 mg, 2.68 mmol, 2.50 equiv), and allyl iodide (206 μL, 377 mg, 2.25 mmol, 2.10 equiv) as an electrophile to afford the title compound as yellow viscous oil, $R_f$ 0.34 (hexanes/EtOAc, 3:1). Yield 148 mg (0.60 mmol, 56%); $^1$H NMR (500.13 MHz, $CDCl_3$) $\delta$ 5.88 (dddd, $J$=17.3, 9.6, 8.2, 6.3 Hz, 1H), 5.79 (ddt, $J$=17.0, 10.1, 5.4 Hz, 1H), 5.27 (dq, $J$=17.0, 1.6 Hz, 1H), 5.14 (br m, 1H), 5.12–5.09 (m, 2H), 3.70–3.66 (m, 8H), 3.98 (dt, $J$=5.3, 1.6 Hz, 2H), 2.62 (dd, $J$=13.9, 6.3 Hz, 1H), 2.40 (dd, $J$=13.9, 8.2 Hz, 1H), 1.43 (s, 3H); $^{13}$C NMR (125.76 MHz, $CDCl_3$) $\delta$ 170.6, 133.9 (+), 132.4 (+), 118.4 (–), 116.2 (–), 83.9, 82.3, 66.8 (–), 66.7 (–), 48.2 (–), 48.1 (–), 44.3 (–), 40.4, 25.7 (–), 23.1 (+); IR (film, cm$^{-1}$): 3076, 2976, 2920, 2854, 1643, 1420, 1209, 1153, 1117, 1030, 916, 505; GC: $t_R$ 10.99 min; HRMS (TOF ES): found 248.1644, calculated for $C_{15}H_{22}NO_2$ (M+H) 248.1650 (2.4 ppm).

## Acknowledgements

Financial support from the University of Kansas and the National Science Foundation (EEC-0310689) is gratefully acknowledged.

## Supplementary data

Spectral charts for all new compounds. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.04.123.

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