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Synthesis and unusual [2+2]-cycloaddition reactions of ethyl 4-chloro-2-oxobut-3-ynoate with unactivated alkenes

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ABSTRACT

The highly activated acetylenes, ethyl 4-chloro-2-oxobut-3-ynoate and ethyl 4-bromo-2-oxobut-3-ynoate, were prepared from readily available bis(trimethylstannyl)acetylene in two steps with high overall yield. An unusual ability of the former to furnish [2+2]-cycloadducts with 1,1-disubstituted alkenes in the absence of irradiation and catalysts was discovered. The cycloaddition of ethyl 4-chloro-2-oxobut-3-ynoate to the 1,2-disubstituted alkenes was shown to be effectively catalyzed with stannic chloride.

1. Introduction

Four-membered carbocycles are important building blocks in the total synthesis of natural products, and are also very reactive and useful tools in many transformations.[1] Cycloaddition reactions are among the most powerful and frequently used methods for the construction of different rings,[2] and the [2+2]-cycloaddition of alkenes and/or alkynes is a simple and versatile strategy in the synthesis of cyclobutane and cyclobutene derivatives.[3] This thermally forbidden process by the Woodward–Hoffman rules,[4] can be achieved photochemically,[5] by thermal radical reactions[6] or by using either Lewis acid catalysts[7] or transition metal catalysts.[8] In the absence of irradiation and a catalyst, the cycloaddition is only possible between unsaturated partners with strong donating and strong accepting substituents, when stepwise mechanism is realized.[9]

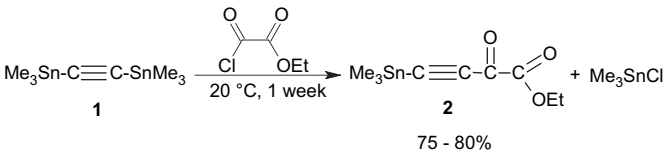
2-Oxo-3-butynoic esters represent an important class of organic compounds due to their unique structure with multiple functional groups and strong activation of the triple bond. Although several methods have been reported for their synthesis,[10] the halogenated acetylenes **3a**, **b** were unknown until now. We expected these compounds to be very reactive in the different cycloadditions and the cycloadducts should be a versatile tool in heterocyclization processes.

In this article, we describe the preparative synthesis and unusual [2+2]-cycloaddition reactions of the halogenated acetylenes **3a**, **b** with simple alkenes.

2. Results and discussion

2.1. The synthesis of ethyl 4-halo-2-oxobut-3-ynoates

After numerous unsuccessful attempts using trimethylsilylacetylene and bis(trimethylsilyl)acetylene we discovered that readily available[11] bis(trimethylstannyl)acetylene **1** reacts with ethyloxalylchloride at ambient temperature to form 2-oxo-4-trimethylstannyl-3-butynoate **2**, which is stable under storage and distillable in vacuum (Scheme 1).



Scheme 1.

Acetylene **2** can be easily halogenated to furnish the target compounds **3a**, **b**. The main challenge at this stage is to separate the halogenated acetylenes from halotrimethylstannanes, simultaneously formed. The purification of compound **3a** can be achieved by washing the reaction mixture with cold water, whereas in the case of **3b**, fraction distillation is necessary, although it leads to decreased yields (Scheme 2).

Acetylenes **3a**, **b** appeared to be relatively stable compounds and can be stored for a prolonged time and distilled in vacuum without decomposition.

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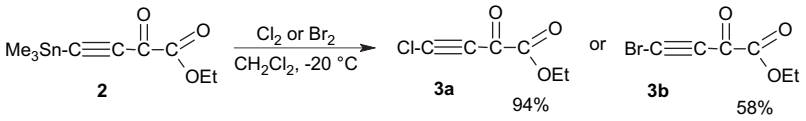


Scheme 2.

2.2. Thermal [2+2]-cycloaddition reactions of ethyl 4-chloro-2-oxobut-3-ynoate with 1,1-disubstituted alkenes

Investigating the reaction of acetylene **3a** with 1,1-disubstituted alkenes, we initially expected to receive the ene addition adducts under mild conditions due to the strong activation effect of the ethoxyoxalyl function. It was found that this reaction indeed takes place even at 60 °C, but to our surprise [2+2]-cycloadducts **4** (head to head) were detected as the major products. Cycloadducts (head to tail) **5** and ene adducts **6** were also formed in small quantities. Fortunately, in some cases it was possible to separate these isomeric substances by column chromatography (Table 1, Scheme 3).

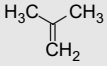
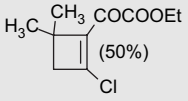
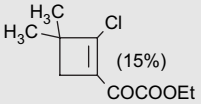
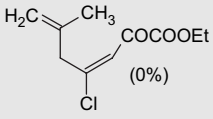
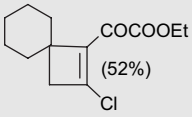
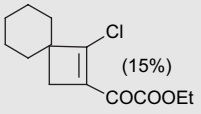
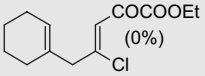
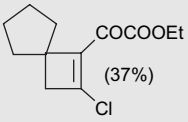
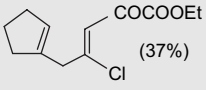
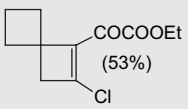
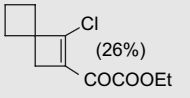
Thus, these cycloaddition reactions do not require either irradiation or catalysts. It was also found that the addition of radical traps has no effect on the rate and direction of the reaction. Polar solvents are known to accelerate considerably [2+2]-dipolar cycloadditions, however, addition of acetonitrile did not result in any apparent acceleration of interactions. The formation of two regioisomers **4** and **5** is also contradicting both the polar and the radical mechanism. The above facts allowed us to suggest that acetylene **3a** undergoes addition to alkenes by a concerted mechanism although it is symmetry forbidden. To overcome this contradiction, we supposed that the bond index of the terminal carbon atom and halogen atom in the molecule **3a** is sharply increased owing to the strong negative mesomeric effect of the ethoxyoxalyl group. The resonance form describing such a redistribution of electron density has ketenium structure, which enables the concerted $[\pi 2_s+\pi 2_a]$-cycloaddition (Scheme 4).

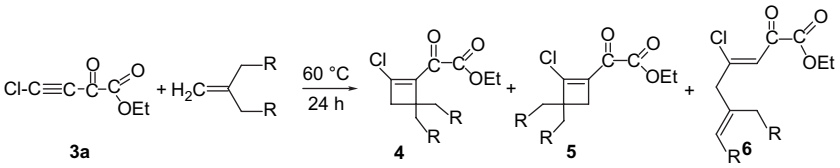
It should be noted that according to the previously published report, acetylenes such as acetylenedicarboxylic esters, hexafluorobutyne-2, 1,1,1-trifluoropropine, and propiolic esters, molecules, which do not contain a mesomeric electron donating substituent at the C≡C– bond, react with simple alkenes under severe conditions to give only ene addition products.[12]

2.3. Catalytic [2+2]-cycloaddition reactions of ethyl 4-chloro-2-oxobut-3-ynoate with 1,2-disubstituted or monosubstituted alkenes

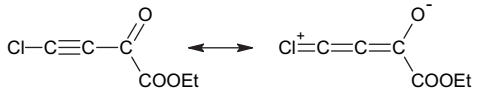
The further studies have shown that acetylene **3a** possesses insufficient electrophilicity for addition to the less reactive monosubstituted and 1,2-disubstituted alkenes. The reaction did not take place below 80–90 °C, whereas the decomposition of the enophile occurred under higher temperature. We discovered, however, that $SnCl_4$ exerts powerful catalytic effect and the cycloadditions were complete within 1–2 h at 0 °C. The process is stereospecific and the resulted cyclobutenes conserve the configuration of the initial alkenes, but not regiospecific and hexene-1 forms two regioisomers in the ratio 5:1 according to the ^{1}H NMR spectroscopy data. A target

Table 1
The reactions of 2-oxo-4-chloro-3-ethylbutynoate **3a** with 1,1-disubstituted alkenes

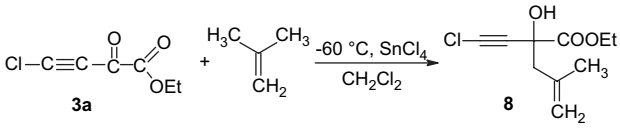
Entry	Alkene	Adduct **4** (head to head) (isolated yield)	Adduct **5** (head to tail) (isolated yield)	Ene adduct **6** (isolated yield)	Ratio **4**/**5**/**6** in reaction mixture (according to ^{1}H NMR spectroscopy)
a		 (50%)	 (15%)	 (0%)	15:3:5
b		 (52%)	 (15%)	 (0%)	20:7:3
c		 (37%)	—	 (37%)	1:0:1
d		 (53%)	 (26%)	—	13:7: 0



Scheme 3.

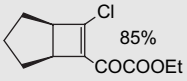
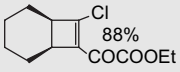
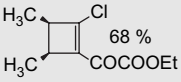
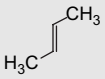
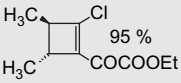
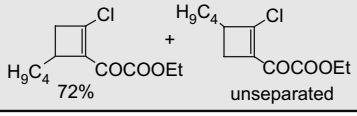


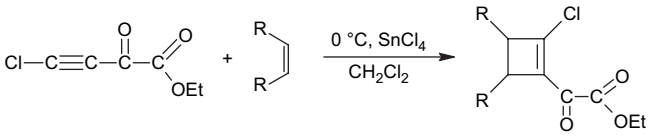
Scheme 4.



Scheme 6.

Table 2
The catalytic reactions of ethyl 4-chloro-2-oxobut-3-ynoate **3a** with 1,2-disubstituted and monosubstituted alkenes

Entry	Alkene	Adduct **7** (isolated yield, %)	Conditions (time)
a		 85%	1.5 h
b		 88%	1 h
c		 68 %	40 min
d		 95 %	15 min
e		 72% unseparated	50 min



Scheme 5.

product **7e** was isolated in a good yield, whereas we were unable to separate the minor compound (head to tail) (Table 2, Scheme 5).

Inspired with these results, we tried to expand the catalytic approach to the reaction of acetylene **3a** with 1,1-disubstituted alkenes but unfortunately only a Prins reaction was found to take place at low temperature to afford alcohol **8**, whereas heating up to 0 °C caused the polymerization of alkene (Scheme 6).

Currently, we do not have a reasonable explanation of such a difference in the reaction ability between 1,2- and 1,1-disubstituted alkenes, but we believe that the thermal and catalytic methodologies complement each other. It should be also noted that all the cycloadducts have the structure of β-chloro–α,β-unsaturated ketones, which are very useful compounds for different heterocyclization reactions.

In order to distinguish the isolated isomers **4** and **5** we have elaborated two simple methods. The first is a reaction with pyridine. We supposed that isomers (head to head) would react with pyridine match faster than the isomers (head to tail) owing to the steric hindrances of the last. Indeed this was shown to be the case: the isomers **4** form pyridinium salts almost quantitatively within 6 h at 20 °C in ether whereas the isomers **5** give only the traces of the products after a week. The second and most convincing evidence is based on that the cycloadducts **4** are enolizable ketones whereas cycloadducts **5** are not. Due to this structural feature isomers **4** undergo rapid H–D-exchange at C-3 center in a solution of DCl/D_2O in dioxane, and the progress of the reaction can be easily monitored by ^1H NMR spectroscopy. Cycloadducts **5** remain unchangeable at these conditions (Scheme 7).

3. Conclusion

The strongly activated acetylenes ethyl 4-chloro-2-oxobut-3-ynoate and ethyl 4-bromo-2-oxobut-3-ynoate were obtained for the first time in two simple steps. An unusual ability of 2-oxo-4-chloro-3-ethylbutynoate to form [2+2]-cycloadducts with 1,1-disubstituted alkenes was discovered. It was also shown that the addition of **3a** to the less reactive 1,2-disubstituted alkenes is effectively catalyzed with stannic chloride.

4. Experimental

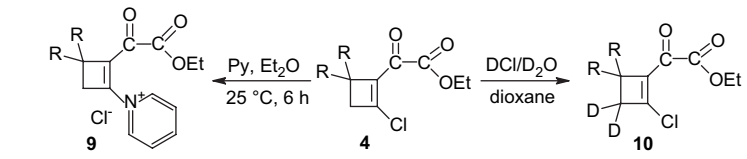
4.1. General

Manipulations with trimethylstannylacetylenes were carried out in an argon atmosphere, though the contact with air within the several seconds is not critical. Ethyl oxalyl chloride was distilled prior to use. Acetylene has been purified by passing through the sulfuric acid and the cooling (dry ice) trap.

4.2. Bis(trimethylstannyl)acetylene (1)

This compound was obtained according to Ref. 12 with some modifications, which allow to simplify the isolation and to increase the yield.

To the vigorously stirred solution of BuLi (1.0 N) in hexane (800 mL) at −35 °C the strong stream of acetylene was introduced until the absorption of the gas has stopped (gas counter at the exit of the system). The reaction mixture was refluxed for 1 h, cooled to



R, R = CH_3 (**9a**), -$(CH_2)_5$- (**9b**) R, R = CH_3 (**10a**), -$(CH_2)_5$- (**10b**)

Scheme 7.

−35 °C and the solution of trimethyltin chloride (160.00 g, 0.80 mol) in 200 mL of hexane was added in one portion to the stirred suspension of lithium acetylenide. The mixture was refluxed and stirred additionally for 1 h and then exposed in argon atmosphere at ambient conditions overnight. The most part of the clear solution was carefully decanted from lithium chloride, the precipitate was diluted with hexane and filtered off. The combined hexane solution was concentrated and the residue was distilled in vacuo with an air condenser in such a rate to prevent the crystallization in the condenser. The distillate quickly solidified on standing. The yield of **1** was 100.00–105.00 g (70.0–74.0%), bp 99–101 °C (10 Torr), mp 58–60 °C (lit.[12] mp 58–60 °C).

4.3. Ethyl 2-oxo-4-(trimethylstannyl)but-3-ynoate (2)

The suspension of acetylene **1** (50 g, 0.14 mol) in ethyl oxalyl chloride (77.5 g, 0.570 mol) was magnetically stirred until the dissolution of the solid was complete, than the solution was stored for 1 week at 25 °C. The excess of ethyl oxalyl chloride and trimethyltin chloride were distilled off at 10 Torr with a short column until the internal temperature reached 70 °C (the distilled mixture can be repeatedly fractionated at atmospheric pressure collecting the major fraction in the temperature interval 128–134 °C and using it in the same synthesis), the dark residue was distilled in the deep vacuum to furnish compound **2** (33.7 g, 82%) as a colorless liquid; bp 95–97 °C (0.6 Torr) (the less deep vacuum may caused the partial decomposition); [Found: C, 37.02; H, 4.80; Sn, 40.80. $C_9H_{14}O_3Sn$ requires: C, 37.42; H, 4.88; Sn, 41.08%.] IR (neat) 2987, 2190, 1748, 1685 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.32 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 1.35 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 0.4 (9H, s, Me_3Sn); δ_C (100.6 MHz, $CDCl_3$) 168.6, 159.3, 110.6, 104.5, 63.0, 13.9, −7.7.

4.3.1. Ethyl 4-chloro-2-oxobut-3-ynoate (**3a**)

To the stirred solution of compound **2** (20.70 g, 0.072 mol) in CH_2Cl_2 (60 mL) at −30 °C the solution of chlorine (5.90 g, 0.083 mol) in CCl_4 (18 mL) was added dropwise. After the warming to the ambient temperature the solvent was removed in vacuum and the residue was diluted with hexane (150 mL). The resultant solution was washed with cold water (3×100 mL), dried with Na_2SO_4, concentrated, and the crude product was distilled to afford acetylene **3a** (9.0 g, 78%) as a colorless liquid; bp 53 °C (1 Torr); [Found: C, 44.59; H, 3.17; Cl, 22.18. $C_6H_5ClO_3$ requires: C, 44.89; H, 3.14; Cl, 22.08%.] IR (neat) 2988, 2195, 1742, 1691, 1141 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.36 (q, 2H, *J* 7.1 Hz, OCH_2CH_3), 1.38 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 168.1, 158.4, 79.8, 67.7, 63.6.

4.3.2. Ethyl 4-bromo-2-oxobut-3-ynoate (**3b**)

To the stirred solution of compound **2** (20.70 g, 0.072 mol) in CH_2Cl_2 (60 mL) at −30 °C the solution of bromine (12.60 g, 0.078 mol) in CH_2Cl_2 (18 mL) was added dropwise. After warming to the ambient temperature the solvent was removed in vacuum and the residue was fractionated on effective column to afford compound **3b** (8.6 g, 58%) as a yellowish liquid; bp 76–77 °C (2 Torr); [Found: C, 34.89; H, 2.52; Br, 39.09. $C_6H_5BrO_3$ requires: C, 35.15; H, 2.46; Br, 38.98%.] IR (neat) 2993, 2199, 1745, 1690 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.38 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 1.39 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 168.1, 158.3, 75.6, 64.5, 63.6.

4.4. General procedure for the thermal [2+2]-cycloaddition reactions of ethyl 4-chloro-2-oxobut-3-ynoate 3a with 1,1-disubstituted alkenes (Table 1)

Compound **3a** (0.49 g, 0.0031 mol) and alkene (0.01 mol) were heated in a sealed ampoule at 60 °C for 24 h. The excess of alkene was removed in vacuum and the residue was chromatographed on a column (silica gel, hexane/AcOEt=20:1).

4.4.1. Ethyl (2-chloro-4,4-dimethylcyclobut-1-en-1-yl)(oxo)-acetate (**4a**)

From **3a** with isobutylene. Pale yellow oil; yield 0.34 g (50%); [Found: C, 55.62; H, 6.22; Cl, 16.18. $C_{10}H_{13}ClO_3$ requires: C, 55.44; H, 6.05; Cl, 16.36%.] R_f=0.3; IR (neat) 2965, 2874, 1742, 1667, 1602 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.33 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.59 (2H, s, –C–CH_2–C=), 1.36 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.33 (6H, s, Me_2C); δ_C (100.6 MHz, $CDCl_3$) 178.6, 162.7, 143.7, 143.1, 62.4, 50.9, 42.7, 24.2, 13.9.

4.4.2. Ethyl (2-chloro-3,3-dimethylcyclobut-1-en-1-yl)(oxo)-acetate (**5a**)

From **3a** with isobutylene. Pale yellow oil; yield 0.10 g (15%); [Found: C, 55.40; H, 6.18; Cl, 16.42. $C_{10}H_{13}ClO_3$ requires: C, 55.44; H, 6.05; Cl, 16.36%.] R_f=0.25; IR (neat) 2960, 2878, 1742, 1667, 1602 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.35 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.56 (2H, s, –C–CH_2–C=), 1.38 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.25 (6H, s, Me_2C); δ_C (100.6 MHz, $CDCl_3$) 178.6, 162.4, 153.4, 132.1, 62.5, 48.0, 40.9, 22.8, 13.8.

4.4.3. Ethyl 1-chlorospiro[3.5]non-1-ene-2-carboxylate (**4b**)

From **3a** with methylenecyclohexane. Pale yellow oil; yield 0.40 g (52%); [Found: C, 60.92; H, 6.69; Cl, 13.85. $C_{13}H_{17}ClO_3$ requires: C, 60.82; H, 6.67; Cl, 13.81%.] R_f=0.3; IR (neat) 2929, 2854, 1744, 1666, 1600 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.33 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.56 (2H, s, –C–CH_2–C=), 1.91 (m), 1.65 (m), 1.50 (m), 1.23 (m) (totally 10H, –$(CH_2)_5$–), 1.35 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.9, 162.9, 144.7, 144.1, 62.4, 48.4, 47.8, 33.2, 25.4, 25.0, 13.9.

4.4.4. Ethyl 2-chlorospiro[3.5]non-1-ene-1-carboxylate (**5b**)

From **3a** with methylenecyclohexane. Pale yellow oil; yield 0.12 g (15%); [Found: C, 60.90; H, 6.71; Cl, 13.88. $C_{13}H_{17}ClO_3$ requires: C, 60.82; H, 6.67; Cl, 13.81%.] R_f=0.25; IR (neat) 2931, 2852, 1738, 1666, 1660 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.42 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.53 (2H, s, –C–CH_2–C=), 1.72 (m), 1.32 (m) (totally 10H, –$(CH_2)_5$–), 1.40 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.5, 162.4, 153.4, 133.1, 62.4, 52.8, 38.8, 32.6, 23.2, 22.0, 14.0.

4.4.5. Ethyl 2-chlorospiro[3.4]oct-1-ene-1-carboxylate (**4c**)

From **3a** with methylenecyclopentane. Pale yellow oil; yield 0.28 g (37%); [Found: C, 60.00; H, 6.22; Cl, 14.23. $C_{12}H_{15}ClO_3$ requires: C, 59.39; H, 6.23; Cl, 14.23%.] R_f=0.3; IR (neat) 2954, 2867, 1740, 1667, 1602 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.36 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.68 (2H, s, –C–CH_2–C=), 2.03 (m), 1.79 (m), 1.67 (m) (totally 8H, –$(CH_2)_4$–), 1.38 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.6, 162.8, 143.2, 140.7, 62.3, 52.5, 52.1, 33.9, 24.4, 13.9.

4.4.6. Ethyl (3Z)-4-chloro-5-cyclopent-1-en-1-yl-2-oxopent-3-enoate (**6c**)

From **3a** with methylenecyclopentane. Pale yellow oil; yield 0.28 g (37%); [Found: C, 59.77; H, 6.22; Cl, 14.26. $C_{12}H_{15}ClO_3$ requires: C, 59.39; H, 6.23; Cl, 14.23%.] R_f=0.1; IR (neat) 2950, 2862, 1738, 1667, 1580 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.03 (1H, s, =C*H*–COCOOEt), 5.63 (1H, s, –CH_2–C*H*=), 4.37 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.35 (s, 2H, =C–CH_2–C=), 2.36 (m), 1.95 (m) (totally 6H, –$(CH_2)_3$–), 1.41 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 180.4, 161.9, 153.5, 137.6, 129.8, 119.4, 62.6, 43.8, 34.5, 32.6, 23.4, 13.9.

4.4.7. Ethyl 2-chlorospiro[3.3]hept-1-ene-1-carboxylate (**4d**)

From **3a** with methylenecyclobutane. Pale yellow oil; yield 0.36 g (53%); [Found: C, 57.52; H, 5.89; Cl, 15.82. $C_{11}H_{13}ClO_3$ requires: C, 57.78; H, 5.73; Cl, 15.50%.] R_f=0.3; IR (neat) 2985, 2871, 1743, 1666, 1595 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.42 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.93 (2H, s, –C–CH_2–C=), 2.65 (m), 2.08 (m) (totally 6H, –$(CH_2)_3$–), 1.43 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.7, 162.8, 143.8, 140.8, 62.4, 50.9, 47.6, 30.2, 16.0, 13.9.

*4.4.8. Ethyl 1-chlorospiro[3.3]hept-1-ene-2-carboxylate (**5d**)*

From **3a** with methylenecyclobutane. Pale yellow oil; yield 0.18 g (26%); [Found: C, 57.62; H, 5.71; Cl, 15.18. $C_{11}H_{13}ClO_3$ requires: C, 57.78; H, 5.73; Cl, 15.50%.] R_f=0.25; IR (neat) 2980, 2874, 1743, 1666, 1595 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.33 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.75 (2H, s, –C–CH_2–C═), 2.35 (m), 2.17 (m), 1.94 (m) (totally 6H, –(CH_2)$_3$–), 1.35 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.2, 162.3, 149.5, 132.9, 62.4, 54.0, 40.3, 28.5, 16.0, 13.9.

4.5. General procedure for stannic chloride catalyzed [2+2]-cycloaddition reactions of 2-oxo-chloro-3-ethylbutynoate (3a) with 1,2-disubstituted alkenes and with hexene-1 (Table 2)

To the stirred solution of **3a** (0.49 g, 0.0031 mol) and alkene (0.0036 mol) in CH_2Cl_2 (25 mL) at 0 °C the solution of $SnCl_4$ (0.80 g, 0.0031 mol) in CH_2Cl_2 (5 mL) was added dropwise. The resultant mixture was stirred at 0 °C for the time specified for the each compound below and than treated with the cold 10% HCl solution (50 mL). The organic layer was separated, then the aqueous phase was extracted with CH_2Cl_2 (20 mL), the combined organic solution was washed with cold water (3×20 mL), dried with Na_2SO_4, concentrated in vacuum, and the crude material was purified by column chromatography (silica gel, hexane/AcOEt=20:1).

*4.5.1. Ethyl 7-chlorobicyclo[3.2.0]hept-6-ene-6-carboxylate (**7a**)*

From **3a** and cyclopentene, reaction time 1.5 h. Pale yellow oil; yield 0.60 g (85%); [Found: C, 56.92; H, 5.53; Cl, 15.04. $C_{11}H_{13}ClO_3$ requires: C, 57.78; H, 5.73; Cl, 15.50%.] R_f=0.5; IR (neat) 2960, 2862, 1740, 1668, 1596, 734 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.31 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.40 (1H, dd, *J* 7.8, 3.4 Hz, C*H*), 3.29 (1H, dd, *J* 7.8, 3.4 Hz, C*H*), 1.73 (m), 1.48 (m) (totally 6H, –(CH_2)$_3$–), 1.29 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.0, 162.3, 145.6, 136.4, 62.4, 53.0, 49.7, 25.6, 24.3, 22.5, 13.9.

*4.5.2. Ethyl 8-chlorobicyclo[4.2.0]oct-7-ene-7-carboxylate (**7b**)*

From **3a** and cyclohexene, reaction time 1 h. Pale yellow oil; yield 0.75 g (88%); [Found: C, 59.77; H, 6.20; Cl, 14.76. $C_{12}H_{15}ClO_3$ requires: C, 59.39; H, 6.23; Cl, 14.61%.] R_f=0.5; IR (neat) 2939, 2866, 1741, 1669, 1595 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.31 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.40 (1H, dd, *J* 10.4, 5.0 Hz, C*H*), 3.08 (1H, dd, *J* 10.4, 5.0 Hz, C*H*), 1.78 (m), 1.48 (m) (totally 8H, –(CH_2)$_4$–), 1.35 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 178.2, 162.3, 147.9, 139.3, 62.3, 46.1, 38.0, 22.7, 21.9, 18.0, 17.9, 13.9.

*4.5.3. Ethyl 2-chloro-3,4-(Z)-dimethylcyclobut-1-ene-1-carboxylate (**7c**)*

From **3a** and *Z*-butene-2, reaction time 40 min. Pale yellow oil; yield 0.45 g (68%); [Found: C, 55.59; H, 6.07; Cl, 16.24. $C_{10}H_{13}ClO_3$ requires: C, 55.44; H, 6.05; Cl, 16.36%.] R_f=0.75; IR (neat) 2977, 1740, 1668, 1597 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.27 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.16 (1H, m, *J* 7.1, 4.75 Hz, C*H*–CH), 3.05 (1H, m, *J* 7.1, 4.75 Hz, CH–C*H*), 1.29 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.08 (3H, d, *J* 7.1 Hz, *Me*), 1.06 (3H, d, *J* 7.1 Hz, *Me*); δ_C (100.6 MHz, $CDCl_3$) 178.6, 162.5, 148.5, 139.5, 62.4, 45.7, 37.7, 13.9, 12.6, 10.8.

*4.5.4. Ethyl 2-chloro-3,4-(E)-dimethylcyclobut-1-ene-1-carboxylate (**7d**)*

From **3a** and *E*-butene-2, reaction time 15 min. Pale yellow oil; yield 0.63 g (95%); [Found: C, 55.07; H, 5.93; Cl, 16.75. $C_{10}H_{13}ClO_3$ requires: C, 55.44; H, 6.05; Cl, 16.36%.] R_f=0.6; IR (neat) 2983, 1741, 1668, 1597 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.28 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 2.62 (1H, dd, *J* 6.7, 1.3 Hz, C*H*–CH), 2.49 (1H, dd, *J* 6.7, 1.3 Hz, CH–C*H*), 1.32 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.21 (3H, d, *J* 6.7 Hz, *Me*), 1.17 (3H, d, *J* 6.7 Hz, *Me*); δ_C (100.6 MHz, $CDCl_3$) 178.7, 162.4, 148.5, 138.3, 62.4, 50.8, 42.9, 16.4, 14.7, 13.9.

*4.5.5. Ethyl 4-butyl-2-chlorocyclobut-1-ene-1-carboxylate (**7e**)*

From **3a** and hexene-1, reaction time 50 min. Pale yellow oil; yield 0.64 g (86%); [Found: C, 58.70; H, 6.87; Cl, 14.85. $C_{12}H_{17}ClO_3$ requires: C, 58.90; H, 7.00; Cl, 14.49%.] R_f=0.6; IR (neat) 2931, 2859, 1741, 1670, 1597, 1236 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.31 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.05 (1H, m, C*H*–Bu), 2.91 (dd, *J* 16.1, 4.6 Hz), 2.39 (dd, *J* 16.1, 1.0 Hz) (totally 2H, CH_2), 1.86 (1H, m, C_3H_7CH), 1.85 (m), 1.24 (m) (totally 6H, –(CH_2)$_3$– from Bu), 1.33 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 0.84 (3H, t, *Me*); δ_C (100.6 MHz, $CDCl_3$) 178.4, 162.5, 143.9, 140.6, 62.4, 41.9, 40.0, 31.8, 29.4, 22.6, 14.0, 13.9.

4.6. Ethyl 2-(chloroethynyl)-2-hydroxy-4-methylpent-4-enoate (8)

This compound was obtained from isobutylene according to the general procedure for 1,2-disubstituted alkenes with the exception that the reaction was carried out at −60 °C for 1 h. Yellowish oil; yield 0.14 g (62%); [Found: C, 55.46; H, 5.98; Cl, 16.37. $C_{10}H_{13}ClO_3$ requires: C, 55.44; H, 6.05; Cl, 16.36%.] R_f=0.2; IR (neat) 3489, 2983, 2226, 1739, 1649, 1210 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.88 (s), 4.78 (s) (totally 2H, –C═CH_2), 4.26 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.58 (OH), 2.64 (2H, m, CH_2), 1.77 (3H, s, ═C–*Me*), 1.31 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 171.5, 139.8, 116.0, 71.2, 68.2, 64.1, 63.2, 47.5, 23.9, 14.0.

4.7. General procedure for preparation of the pyridinium salts (9)

To the solution of pyridine (3.30 mmol) in Et_2O (1.50 mL) compound **4a** or **4b** (3.00 mmol) was added and the resultant solution was stirred at 25 °C for 6 h. The solid salt was filtered off, washed with ether, and dried in vacuum.

*4.7.1. 1-{2-[Ethoxy(oxo)acetyl]-3,3-dimethylcyclobut-1-en-1-yl}pyridinium chloride (**9a**)*

White solid; mp 147–149 °C; yield 0.83 g (94%); [Found: C, 61.07; H, 5.98; Cl, 11.67; N, 5.01. $C_{15}H_{18}ClNO_3$ requires: C, 60.91; H, 6.13; Cl, 11.99; N, 4.74%.]; δ_H (400 MHz, CD_3CN) 9.46 (2H, d, *H*-C^2 arom.), 8.89 (1H, t, *H*-C^4 arom.), 8.40 (2H, t, H-C^3 arom.), 4.47 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.08 (2H, s, C–CH_2–C═), 1.51 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.41 (6H, s, Me_2C); δ_C (100.6 MHz, CD_3CN) 182.4, 164.3, 156.2, 148.2, 146.4, 144.1, 134.7, 64.3, 56.7, 44.2, 17.0, 15.6.

*4.7.2. 1-{1-[Ethoxy(oxo)acetyl]spiro[3.5]non-1-en-2-yl}pyridinium chloride (**9b**)*

White solid; mp 154–155 °C; yield 0.97 g (96%); [Found C, 64.45; H, 6.93; Cl, 10.75; N, 4,46. $C_{18}H_{22}ClNO_3$ requires: C, 64.38; H, 6.60; Cl, 10.56; N, 4.17%.] δ_H (400 MHz, CD_3CN) 9.49 (2H, d, *H*-C^2 arom.), 8.90 (1H, t, *H*-C^4 arom.), 8.44 (2H, t, *H*-C^3 arom.), 4.46 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 3.11 (2H, s, C–CH_2–C═), 1.99 (m), 1.70 (m), 1.24 (m) (totally 10H, –(CH_2)$_5$–); 1.50 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, CD_3CN) 181.9, 164.0, 158.5, 148.7, 145.4, 144.2, 134.2, 64.0, 56.2, 47.3, 35.9, 30.2, 27.4, 16.1.

4.8. General procedure for preparation of deuterium labeled compounds (10)

To the solution of D_2O (2.00 g) and DCl (0.20 g) in dioxane (6.00 mL) compound **4a** or **4b** (3.00 mmol) was added and the resultant solution was exposed for 12 h at 25 °C. The most part of D_2O and dioxane was removed in vacuum, the residue was diluted with ether (10.00 mL), successively washed with the solution of NaOAc (1 g) in D_2O (5.00 mL) and D_2O (5.00 mL), dried over Na_2SO_4, and concentrated in vacuum. The resultant compounds **10a**, **b** had about 96–97%-deuterium purity at C-3 center.

*4.8.1. Ethyl (2-chloro-3,3-dideuterio-4,4-dimethylcyclobut-1-en-1-yl)(oxo)acetate (**10a**)*

Yellow oil; yield 0.58 g (88%); [Found: C, 55.62; H, D, 6.22; Cl, 16.18. $C_{10}H_{11}D_2ClO_3$ requires: C, 55.44; H, D, 6.05; Cl, 16.36%.] IR (neat): 1742, 1671, 1605 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.31 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 1.36 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.30 (6H, s, $(CH_3)_2C$); δ_C (100.6 MHz, $CDCl_3$) 178.6, 162.6, 143.3, 142.9, 62.4, 50.8, 41.80 (quint, J_{CD} 24.5 Hz, CD_2–C), 24.0, 13.9.

*4.8.2. Ethyl 2-chloro-3,3-dideuterio-spiro[3.5]non-1-ene-1-carboxylate (**10b**)*

Yellow oil; yield 0.71 g (91%); [Found: C, 60.01; H, D 7.31; Cl, 13.57. $C_{13}H_{15}D_2ClO_3$ requires: C, 60.35; H, D 7.39; Cl, 13.70%.] IR (neat): 1742, 1671, 1606 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.33 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 1.88 (m), 1.66 (m), 1.58 (m), 1.20 (m) (totally 10H, $-(CH_2)_5-$), 1.35 (3H, t, *J* 7.1 Hz, OCH_2CH_3); δ_C (100.6 MHz, $CDCl_3$) 179.3, 162.8, 144.3, 144.1, 62.5, 48.3, 47.1, 33.2, 25.4, 25.0, 13.9.

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