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1-Ethoxyoxalyl-2-chloroacetylene as a New Dienophile in Diels–Alder Reactions

A. B. Koldobskii, E. V. Solodova, I. A. Godovikov, and V. N. Kalinin

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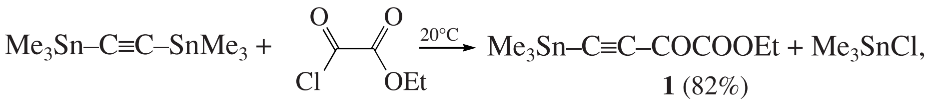
Acetylene dienophiles and enophiles containing two activating substituents one of which is a halogen are of great interest not only for theory but also as substrates in the synthesis of biologically active compounds [1, 2]. Previously, we obtained halogenated trifluoroacetylacetylenes and studied their reactions with different dienes [3], alkenes [4], and vinyl ethers [5]. Acetylenes activated by the alkoxyoxalyl group are a very promising class of compounds in terms of synthesis because of unique possibilities of their functionalization; however, these compounds have been studied only over the past fifteen years and their properties are inadequately understood [6–9].

Within this class of compounds, special attention is attracted by alkynes containing a halogen atom as a second substituent to provide strong activation in cycloaddition reactions followed by the substitution of the halogen by different nucleophiles. However, such acetylenes have not hitherto been obtained and their synthetic possibilities have remained unclear.

In an attempt to solve this problem, we found that the addition of lithium chloroacetylenide to various oxalic acid derivatives and the catalyzed acylation of bis(trimethylsilyl)acetylene were unsuccessful. Readily available [10] bis(trimethylstannyl)acetylene was found to undergo acylation with ethoxyoxalyl chloride at 20°C in the absence of a solvent and catalyst to give 1-ethoxyoxalyl-2-trimethylstannylacetylene **1**, a stable compound distillable in vacuum:



where the product yield is given parenthetically.

The chlorination of compound **1** proceeds rapidly even at low temperature to give 1-ethoxyoxalyl-2-chloroacetylene **2** in high yield. The attempted separation of the target compound from trimethyltin chloride by distillation results in considerable loss; however, the latter compound can be readily removed by washing of the reaction mixture with water:

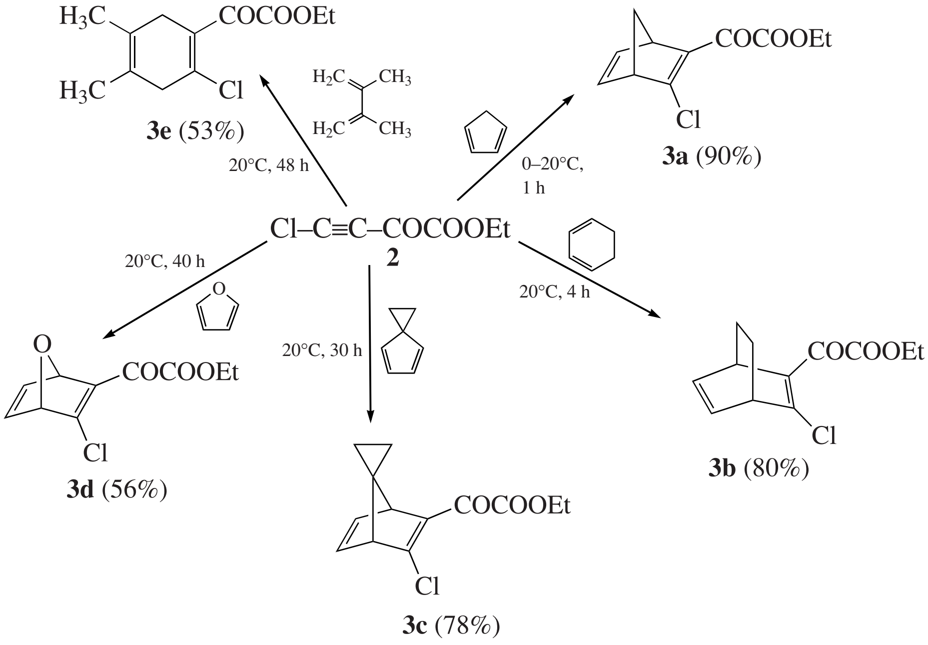
$$\underset{\mathbf{1}}{\mathrm{Me_3Sn{-}C{\equiv}C{-}COCOOEt}} + \mathrm{Cl_2} \xrightarrow{-20^\circ\mathrm{C}} \underset{\mathbf{2}\ (90\%)}{\mathrm{Cl{-}C{\equiv}C{-}COCOOEt}} + \mathrm{Me_3SnCl}.$$

Further studies showed that acetylene **2** is a reactive dienophile and readily undergoes the Diels–Alder reaction with different dienes to produce corresponding cycloadducts **3**. The reaction proceeds rapidly even at 20°C and is complete in 1 h in the case of cyclopentadiene, whereas it takes 48 h for the addition of less reactive 2,3-dimethylbutadiene to be complete. Cycloadduct **3a** can easily be isolated from the reaction mixture by vacuum distillation, whereas other cycloadducts are isolable preferably by chromatography. Furan, a heterocyclic diene, also reacts under mild conditions with acetylene **2**; however, we char-

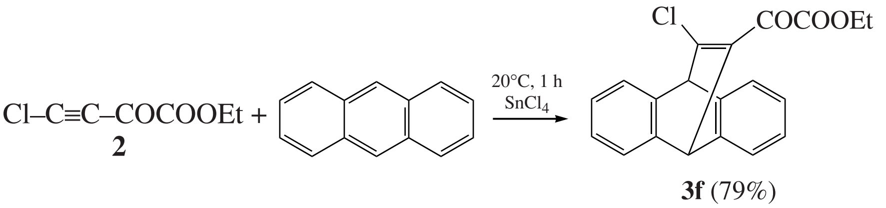
Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, ul. Vavilova 28, Moscow, 119991 Russia

acterized substituted oxanorbornadiene **3d** and determined its yield only by ^{1}H NMR in a dioxane solution. The compound undergoes fast resinification in a pure state even at 0°C.

Scheme 1.



Initially, we failed to carry out the addition reaction of acetylene **2** with anthracene: the reaction did not proceed at ambient temperature, whereas the decomposition of the dienophile was observed on heating to 90–100°C. We found, however, that the reaction is very efficiently catalyzed by stannic chloride and is complete in 1 h at 20°C. Such a strong acceleration of the reaction seems to be explained by an increase in the electrophilicity of the –C≡C– bond as the tin atom in the Lewis acid is chelated by the 1,2-dicarbonyl system of the dienophile:



It is noteworthy that all cycloadducts **3a**–**3f** contain a reactive chlorine atom and ethoxyoxalyl group in a fixed cisoid conformation, which opens wide possibilities for the synthesis of different heterocycles containing carbocyclic fragments and ester group.

EXPERIMENTAL

All experiments with trimethylstannylacetylenes were carried out under an argon atmosphere with the use of anhydrous solvents. Ethoxyoxalyl chloride was distilled immediately prior to use. The structure of the compounds obtained was confirmed by elemental analysis data, ^{1}H and ^{13}C NMR, and IR spectroscopy.

Bis(trimethylstannyl)acetylene. The compound was obtained by the well-known procedure [10] with certain modifications that allowed us to increase the yield and facilitate the isolation of the product.

Acetylene was passed through a solution of *n*-butyllithium (800 mL, 0.8 mol, *c* = 1 mol/L) in hexane with cooling to –35°C and vigorous stirring until absorption of the gas ceased, and the mixture was heated under reflux with stirring for 1 h. A solution of 160 g (0.8 mol) of trimethyltin chloride in 200 mL of hexane was added in one portion to the resultant suspension of lithium acetylenide at –35°C, the mixture was heated under reflux for 1 h, and the reaction mixture was kept for 12 h at 20°C. The precipitate of lithium chloride was filtered off, the filtrate was concentrated in vacuum, and the residue was distilled with the use of an air-cooled condenser to give 101.5 g (71%) of bis(trimethylstannyl)acetylene, bp 100°C (8 mmHg), mp 58–60°C (lit. [10]: mp 58–60°C).

1-Ethoxyoxalyl-2-trimethylstannylacetylene 1. A solution of 50 g (0.14 mol) of bis(trimethylstannyl)acetylene in 77.56 g (63.5 mL, 0.57 mol) of ethoxyoxalyl chloride was kept at 20°C for 8 days. Excess ethoxyoxalyl chloride and resulting trimethyltin chloride were distilled off in a vacuum of 10–15 mmHg (the obtained distillate may be redistilled at atmospheric pressure collecting a fraction with bp 128–134°C that contains about 90% of ethoxyoxalyl chloride and can be reused in the same reaction) until the distillation residue temperature rose to 70°C. The residue was distilled to give 33.7 g (82%) of compound **1**, bp 95°C (0.5 mmHg). Distillation at higher pressure leads to the partial decomposition of the compound and a sharp decrease in the yield.

1-Ethoxyoxalyl-2-chloroacetylene 2. A solution of 6.1 g of chlorine in 18 mL of carbon tetrachloride was added dropwise to a solution of 20.70 g (0.072 mol) of acetylene **1** in 35 mL of methylene chloride at –35°C. The mixture was stirred for 20 min at 20°C, and the main amount of CCl_4 was removed in vacuum at 20°C. The residue was diluted with 150 mL of hexane and washed with cold water (3 × 100 mL), the organic layer was dried with anhydrous Na_2SO_4 and concentrated in vacuum, and the residue was distilled to give 9.0 g (78%) of compound **2**, bp 53°C (1 mmHg).

General procedure of the synthesis of compounds 3a–3e. A solution of 0.49 g (0.4 mL, 0.0031 mol) of 1-ethoxyoxalyl-2-chloroacetylene **2** and 0.0043 mol of a diene in 5 mL of methylene chloride was kept at 20°C for different times (see Scheme 1) and the solvent was removed in vacuum. Cycloadduct **3a** was isolated by vacuum distillation; other cycloadducts were isolated by column chromatography (silica gel, eluent used was an ethyl acetate–hexane (1 : 20) mixture).

2-Ethoxyoxalyl-3-chlorobicyclo[2.2.1]heptadiene-2,5 3a. The compound was obtained by the general procedure from acetylene **2** and cyclopentadiene. Reaction time 1 h, yield 0.63 g (90%), bp 110°C (2 mmHg).

2-Ethoxyoxalyl-3-chlorobicyclo[2.2.2]octadiene-2,5 3b. The compound was obtained by the general procedure from acetylene **2** and 1,3-cyclohexadiene. Reaction time 4 h, $R_f = 0.3$. Yield 0.60 g (80%).

2-Ethoxyoxalyl-3-chlorobicyclo[2.2.1]hepta-2,5-diene-7-spiro-1'-cyclopropane 3c. The compound was obtained by the general procedure from acetylene **2** and spiro[2,4]hepta-4,6-diene. Reaction time 30 h, $R_f = 0.27$. Yield 0.55 g (72%).

2-Ethoxyoxalyl-3-chloro-7-oxabicyclo[2.2.1]heptadiene-2,5 3d. The compound was obtained by the general procedure from acetylene **2** and furan in 2 mL of 1,4-dioxane. Reaction time 40 h, yield 56% (according to ^{1}H NMR). The compound is stable only in solution.

1-Ethoxyoxalyl-2-chloro-4,5-dimethylcyclohexadiene-1,4 3e. The compound was obtained by the general procedure from acetylene **2** and 2,3-dimethylbutadiene. Reaction time 48 h, $R_f = 0.25$. Yield 0.40 g (53%).

Ethyl (12-chloro-9,10-dihydro-9,10-ethenoanthracen-11-yl)(oxo)acetate 3f. A solution of 0.36 mL (0.8 g, 0.0031 mol) of tin tetrachloride in 5 mL of methylene chloride was added dropwise to a solution of 0.6 g (0.0034 mol) of anthracene and 0.4 mL (0.49 g, 0.0031 mol) of acetylene **2** in 25 mL of the same solvent with stirring at 20°C. The mixture was stirred for 1 h at 20°C and treated with 60 mL of 5% aqueous hydrochloric acid. The organic layer was separated, and the aqueous layer was extracted with 20 mL of methylene chloride. The combined organic extracts were washed with cold water (3 × 20 mL), dried with Na_2SO_4, and concentrated in vacuum, and the residue was chromatographed on a column (ethyl acetate–benzene (1 : 20) mixture as eluent). $R_f = 0.95$, yield 0.83 g (79%).

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