Synthesis of 3-Alkylseleno-2-cylcobutenone via [2+2] Cycloaddition Reaction of Alkyneselenolate with Diphenylketene

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Received 27 February 2002

Abstract: 3-Alkylseleno-2-cyclobutenones were synthesized by reaction of alkyneselenolate with diphenylketene via [2+2] cycloaddition. The complete structure of the 2-cyclobutenone was determined by X-ray diffraction.

Key words: [2+2] cycloaddition, 3-alkylseleno-2-cyclobutenone, alkyneselenolate, ketene, X-ray diffraction

Cyclobutenones have emerged as versatile synthons and interesting electrocyclic ring reactions[1] as well as being useful for the construction of complex organic compounds in recent years.[2] They are also interesting for their reactivity and have been examined by way of computational calculations.[3]

We are interested in the synthesis of novel cyclic compounds containing selenium.[4] We have reported the synthesis of β-selenolactam from alkyneselenolate.[5] The use of alkyneselenolate is one of the most efficient methods for the synthesis of cyclic compounds containing selenium.[6] A review details ketene cycloaddition.[7] The synthesis of 3-ethoxy-2-cyclobutenone using ketene has been often reported,[8] while there is no report of the synthesis of 3-alkylseleno-2-cyclobutenone according to our best knowledge. Herein, we describe a facile preparation of a series of 3-alkylseleno-2,4,4-triphenyl-2-cyclobutenone via [2+2] cycloaddition by the reaction of alkyneselenolate with diphenylketene.[9]

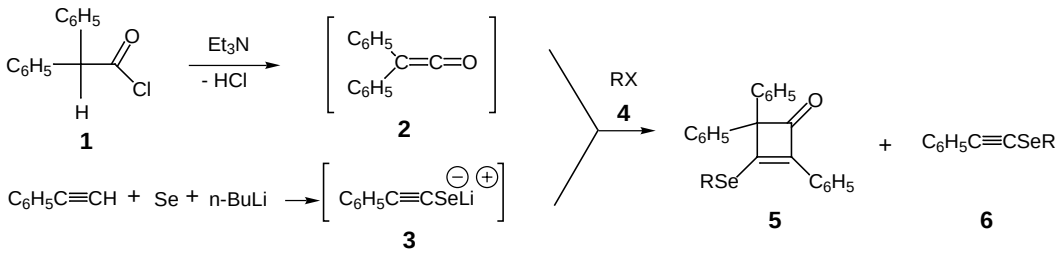
Diphenylketene **2** has been prepared by dehydrohalogenation of substituted acetyl chloride in the presence of a base in situ. Lithium alkyneselenolate **3** was added into the reaction mixture. Finally cyclic compound, 3-alkylseleno-2,4,4-triphenyl-2-cyclobutenone **5**, was obtained by the trapping with alkyl halides **4** in 38–67% yields (Table). Alkyl phenylethynyl selenide **6**, which was generated by the reaction of **3** with **4** directly, was obtained as a byproduct (Scheme 1). At first, structure of **5** could not be determined only by NMR and mass spectra. Therefore, the single crystals were prepared and were subjected to X-ray diffraction for the structure determination. Finally, the absolute structure of **5** was confirmed by studies of IR, MS, ^{1}H, ^{13}C and ^{77}Se NMR spectra, elemental analysis and X-ray diffraction.[10]

Table Synthesis of 3-Alkylseleno-2,4,4-triphenyl-2-cyclobutenone **5**

Reactant	RX	Product	Yield (%)
4a	CH_3I	**5a**	51
4b	C_2H_5I	**5b**	52
4c	C_3H_7I	**5c**	56
4d	C_4H_9I	**5d**	67
4e	$C_6H_5CH_2Br$	**5e**	38
4f	$C_6H_5CH_2CH_2Br$	**5f**	55

Several attempts to determine the optimal conditions for improvement of the yield of **5b** were carried out. The reaction for 1 h at room temperature gave **5b** in 52% yield. Longer reaction time and higher temperature failed to improve the yield of **5b**.

Several 3-alkylseleno-2,4,4-triphenyl-2-cyclobutenones **5** were prepared by using the corresponding alkyl halides **4**.

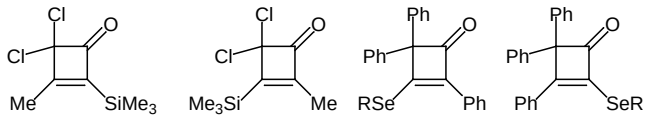


Scheme 1

Synlett 2002, No. 5, 03 05 2002. Article Identifier:
1437-2096,E;2002,0,05,0805,0807,ftx,en;Y02802ST.pdf.

ISSN 0936-5214

Longer alkyl group gave higher yield of **5** (Table). In the case of the Moore cyclization enyne-ketenes, generally, higher temperature, for example more than 100 °C or refluxing, was used for the preparation of desired products.[11] In the present reaction, milder conditions, i.e. room temperature, gave the best result. Studies by Danheiser and co-workers demonstrated that dichlorocyclobutenones could be prepared by the addition of dichloroketene to trialkylsilylacetylenes.[12] Among their results, addition of dichloroketene to methyl (trimethylsilyl)acetylene resulted in the formation of two regioisomeric products in a ratio of 64:36 (**7** and **8** in Figure 1). The reactions of ethoxy(trimethylsilyl)acetylene and phenyl(trimethylsilyl)acetylene with dichloroketene led exclusively to a single cycloadduct like type **7**.[13]



7 **8** **5** **5'**

Figure 1

In the present reaction, only a single product was obtained. The X-ray diffraction study of the product clearly showed that the crystals were not **5′** but **5** (Figure 2 and Scheme 2).[14] The bond length of C2-C3 is 1.375 Å and indicates a double bond. The sum of the three angles around each of the C1, C2 and C3 atoms is almost 360.0°, respectively. Therefore, the arrangement of C1, C2, C3 C4, O1, Se1 and C19 atoms is almost planar.

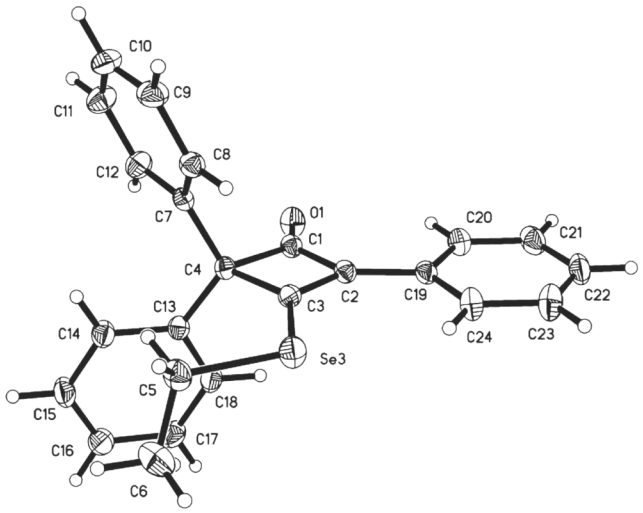
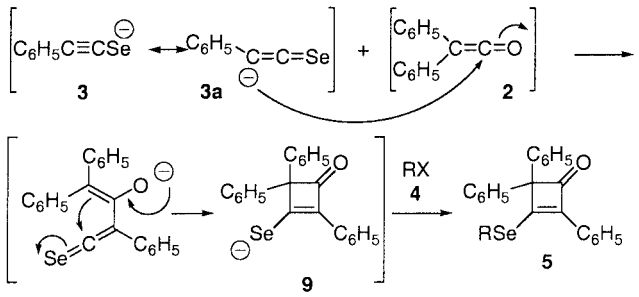


Figure 2 ORTEP diagram (50% thermal ellipsoids) of compound **5b**.

The reaction of phenylethynyl selenide **6** with diphenylketene **2** provided no products other than recovered



Scheme 2

starting materials. The reaction without alkyl halide gave only mixtures instead of 3-selenoxocyclobutanone, while it has been reported that a 1,3-cyclobutanedione could be easily isolated.[8a] Because 3-selenoxocyclobutanone was unstable, the stable product **5**, which is the enolate form, was only obtained when **9** was trapped with haloalkane **4**. From these results the formation of **5**, could be explained by the addition of the nucleophilic site of alkyne **3a** to the most electron deficient site, the carbonyl carbon, of the ketene **2** presented in Scheme 2. That is, in the case of the present reaction, the electron of resonance structure **3a** attacked only the center carbon of ketene **2** via the [2+2] cycloadduct **9** affording the single product **5** but neither **5′** nor a mixture of **5** and **5′**. The reaction of lithium alkyneselenolate **3** (LiSeCCPh) with acyl chloride (RCOCl) gave *Se*-alkynyl selenocarboxylate (RCOSeCCPh) by nucleophilic addition of the selenium of **3** to the carbonyl carbon of acyl chloride.[15] On the other hand, the reaction of **3** (LiSeCCPh) with alkylidenamine ($RCH = NR_1$) afforded β-selenolactam by addition of the most nucleophilic site of alkyne **3a**.[5] Furthermore, the reactions of lithium alkynethiolate (LiSCCPh) and lithium ynolate (LiOCCPh) with carbonyl compound proceeded by addition of the most nucleophilic site of alkyne to the carbonyl carbon of the carbonyl compound.[16] The present reaction obeys the latter. Acetylenes bearing transition metal, silyl, germyl, arsenyl and phosphoryl substituents could serve as substrates for the [2+2] cycloaddition with ketene. The regiochemistry of cycloaddition involving organometallic acetylene was generally seen with simpler alkynes, but silylalkylacetylenes gave both possible regioisomers (Figure 1).[13,17] The present reaction using alkyneselenolate was the former.

Though many reviews have devoted exclusively to ketene cycloaddition,[7,18] according to our best knowledge, this is the first example of the reaction of ketene with alkyneselenolate.

Acknowledgement

We thank Dr. Dale Swenson, of the University of Iowa, Chemistry Department X-ray Diffraction Facility, for his assistance in acquiring X-ray crystallographic data.

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(9) This work was first reported at the 222nd National Meeting of the American Chemical Society, Chicago, August 26-30, 2001.

(10) **Procedure**: 3-Methylseleno-2,4,4-triphenyl-2-cyclobutenone **5a**: Lithium alkyneselenolate **3** (2 equiv), generated in situ from phenylacetylene (2 equiv), *n*-BuLi (2 equiv) and elementary selenium (2 equiv.), was added to THF solution of diphenylketene **2** which was generated from diphenylacetyl chloride **1** (1 equiv) and triethylamine (1 equiv) under argon atmosphere. Moreover, methyl iodide **4a** (2 equiv) was added to the mixture and was stirred at room temperature for 1 h. The mixture was extracted with diethyl ether and washed with saturated NaCl solution. The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by flash chromatography on silica gel with *n*-hexane–diethyl ether (50:1) to give 0.20 g of **5a** (51%) as pale yellow crystals; mp 120.9–122.3 °C; IR (KBr) 1734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.12 (s, 3 H, CH_3), 7.27–7.47 (m, 13 H, Ar), 7.79 (d, *J* = 7.6 Hz, 2 H, Ar); ^{13}C NMR ($CDCl_3$) δ 7.9, 81.7, 127.1, 127.5, 128.2, 128.5, 128.6, 128.8, 129.8, 138.7, 145.7, 169.2, 185.3; ^{77}Se NMR ($CDCl_3$) δ 257.8; MS (CI): *m/z* = 391 [M^+ + 1]; Anal. Calcd for $C_{23}H_{18}OSe$: C, 70.95; H, 4.66. Found: C, 70.63; H, 4.66%. 3-Ethylseleno-2,4,4-triphenyl-2-cyclobutenone **5b**: Pale yellow crystals; mp 111.4–113.2 °C; IR (KBr) 1741cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (t, *J* = 7.6 Hz, 3 H, CH_3), 2.86 (q, *J* = 7.6 Hz, 2 H, CH_2), 7.27–7.48 (m, 13 H, Ar), 7.80 (d, *J* = 7.6 Hz, 2 H, Ar); ^{13}C NMR ($CDCl_3$) δ 14.7, 22.4, 81.6, 127.2, 127.5, 128.3, 128.5, 128.6, 129.9, 138.8, 145.2, 169.7, 185.4; ^{77}Se NMR ($CDCl_3$) δ 349.2; MS (CI): *m/z* = 405 [M^+ + 1]; Anal. Calcd for $C_{24}H_{20}OSe$: C, 71.46; H, 5.00. found: C, 71.10; H, 5.01%.

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