ISSN 1070-4280, Russian Journal of Organic Chemistry, 2013, Vol. 49, No. 11, pp. 1720–1721. © Pleiades Publishing, Ltd., 2013.
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SHORT
COMMUNICATIONS

Cross-Coupling of 2,5-Bis(chloromethylidene)-1,4-dithiane with Phenylacetylene as an Example of Preparation of Symmetric Bridging Bisenyne Compounds

A. V. Martynov, N. A. Makhaeva, and S. V. Amosova

Faworsky Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences,
Irkutsk, 664033 Russia
e-mail: amosova@irioch.irk.ru

Received July 10, 2013

DOI: 10.1134/S1070428013110304

The discovery of highly efficient fungicidal preparations [1] and antibiotics with strongest antitumor activity [2] have stimulated within last 20 years the interest to the chemistry of conjugated enynes. One of the most convenient methods of the synthesis of these compounds is the cross-coupling of vinyl halides and triflates with terminal acetylenes in the presence of palladium catalysts, CuI, and amines as bases (Sonogashira reaction) [3]. An example is known of the preparation of bisenyne sulfide, *cis*-isomer of bis(1-buten-3-ynyl) sulfide by the reaction of diacetylene with H_2S in liquid ammonia [4].

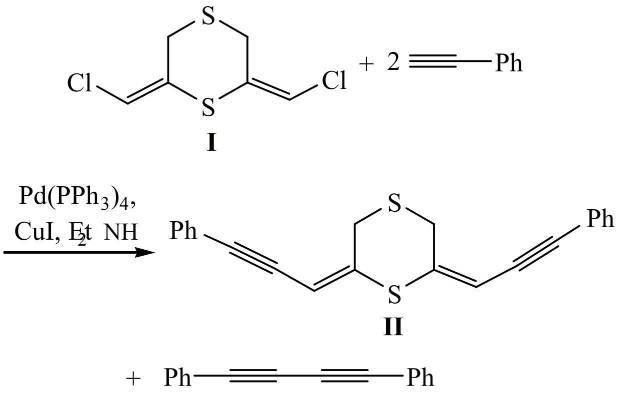
We formerly developed an efficient preparation procedure for *E,E*-isomers of bis(chloromethylidene) derivatives of 1,4-dithiane and its selenium analogs, 1,4-thiaselenane and 1,4-diselenane [5], which were essentially cyclic bis[(*E)*-2-chlorovinyl) chalcogenides. In order to test the possibility to use these compounds in the synthesis of enyne compounds we carried out the reaction of 2,6-bis[(*E*)-chloromethylidene]-1,4-dithiane (**I**) with phenylacetylene under the conditions of Sonogashira reaction.

In the presence of tetrakis(triphenylphosphine) palladium, copper iodide, and diethylamine at room temperature the cross-coupling occurs at two chloromethylidene groups of dithiane **I** with the formation of a symmetric bisenyne compound, 2,6-bis[(*E*)-3-phenylprop-2-ynylidene]-1,4-dithiane (**II**) in 38% yield. 1,4-Diphenylbutadiyne (**III**) was obtained as a side product. Heterocycle **II** and diacetylene **III** were separated by preparative thin layer chromatography on silica gel at the elution with a hexane–chloroform mixture, 1 : 1.

The structure of heterocycle **II** was confirmed by the ^1H NMR spectrum where besides the phenyl ring the signals of bis(methylidene)-1,4-dithiane fragment were observed, and the signal of vinyl proton (δ 5.87 ppm) was shifted upfield with respect to the signal of initial dithiane **I** (δ 6.29 ppm), and the signal of the methylene proton (δ 3.91 ppm) was slightly displaced downfield compared to the respective signal of the initial 1,4-dithiane (δ 3.73 ppm). In the ^{13}C NMR spectrum the bis(methylidene)-1,4-dithiane fragment gave rise to a doublet of triplets of carbon atoms of the group =CH (δ 107.06 ppm) shifted upfield compared to the respective signal of the initial 1,4-dithiane (115.56 ppm [5]), and to a triplet of multiplets signal from the methylene groups (δ 31.79 ppm) slightly shifted downfield with respect to the corresponding signal of initial heterocycle **I** (29.76 ppm [5]). Therewith a sharp difference in the coupling constants of the *sp*^{2}-hybridized carbon atom of the =CH group was observed in heterocycle **II** ($^1J_{CH}$ 167.4 Hz) and initial dithiane **I** ($^1J_{CH}$ 200 Hz [5]) because of the effect of substituent bound to this carbon atom (chlorine atom in случае dithiane **I** and ethynyl fragment in dithiane **II**) [6]. Since the Sonogashira reaction is stereoselective and proceeds without changes in the stereochemistry of the initial ethane [3, 7], (*E,E*)-structure of initial dithiane **I** is conserved in heterocycle **II**.

The formation of diphenyldiacetylene **III** was confirmed by the mass spectrum identical to the known spectrum [8]. We failed to obtain the mass spectrum of heterocycle **II** apparently due to its instability against the electron impact.

Compound **II** is an example of a bisenyne structure where two enyne fragments are separated by a sulfide



III

bridge included in the 1,4-dithiane ring. In contrast to the known bis(1-buten-3-ynyl) sulfide where the triple bond is located in the *cis*-position with respect to the sulfide bridge [4], in heterocycle **II** a *trans*-structure is present.

2,6-Bis[(*E*)-3-phenylprop-2-ynylidene]-1,4-dithiane (II). To 116 mg (0.10 mmol) of Pd(PPh$_3$)$_4$ and 29 mg (0.15 mmol) of CuI in 2 mL of dioxane under an argon atmosphere was added a solution of 290 mg (4.0 mmol) of Et$_2$NH in 0.5 mL of dioxane, the mixture was stirred for 15 min, and then a solution of 107 mg (0.50 mmol) of dithiane in 2.5 mL of dioxane was added, and 30 min later was introduced a solution of 306 mg (3.0 mmol) of phenylacetylene in 1 mL of dioxane. The reaction mixture was stirred at room temperature for 24 h, diluted with 15 mL of water, extracted with chloroform, the extract was dried with CaCl$_2$. On removing chloroform in a vacuum the residue (0.526 g) was chromatographed on silica gel, eluents hexane, then chloroform. We obtained 0.118 g of diphenyldiacetylene **III**, fine white crystals, mp 89°C (87–88ºC [8]) and 0.160 g of a mixture of heterocycle **II** and diphenyldiacetylene in the 1 : 1 ratio according to ^{1}H NMR data (calculated yield of heterocycle **II** 58%]. The obtained mixture of heterocycle **II** and 1,4-diphenylbutadiyne was separated by thin layer preparative chromatography on silica gel, eluent hexane–chloroform, 1 : 1.

Dithiane II. Yield 66 mg (38%), light yellow plate crystals, mp 132–134°C, R_f 0.10–0.28. ^{1}H NMR spectrum, δ, ppm: 3.91 s (4H, CH$_2$), 5.87 s (2H, =CH), 7.31–7.36 m (6H), 7.41–7.47 m (4H). ^{13}C NMR spectrum, δ, ppm: 31.79 t.m (CH$_2$, ^1J 147.1 Hz), 85.16 s (C≡), 96.03 m (C≡), 107.06 d.t (SC=$\underline{\text{CH}}$, ^1J 167.4, ^3J 4.4 Hz), 123.10 s (C^i), 128.57 d (C^3_{arom}, ^1J 160.0 Hz), 128.69 d (C^4_{arom}, ^1J 161.4 Hz), 131.63 d (C^2_{arom}, ^1J 162.6 Hz), 143.26 m (=C–S). Found, %: C 76.98; H 4.64; S 18.38. $C_{22}H_{16}S_2$. Calculated, %: C 76.79; H 4.68; S 18.62. Diphenyldiacetylene **III**, mass spectrum, *m/z* (I_{rel}, %): 202 (100) $[M]^+$, 150 (9), 101 (9).

The main results were obtained on the equipment of the Baikal analytical center in general use of the Siberian Branch of the Russian Academy of Sciences. ^{1}H (400.13 MHz) and ^{13}C (100.61 MHz) NMR spectra were registered on a spectrometer Bruker DPX-400 in CDCl$_3$, internal reference TMS (^{1}H, ^{13}C). Mass spectra were obtained on a GC-MS instrument Shimadzu QP5050A (EI, 70 eV), column SPB-5 ms (60 m).

ACKNOWLEDGME

The study was carried out under the financial support of the Russian Foundation for Basic Research (grant no. 11-03-00810).

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