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Synthesis of β-cyanovinylsulfones

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Abstract

Two separate methods for the preparation of 3-arylsulfonyl-2-butenenitriles (β-cyanovinylsulfones) have been proposed. The first one represented an interaction of sodium arylsulfinates with 2,3-dibromobutanenitrile at 70ºC for 8 hours under pressure in water/alcohol medium (1:1) in the presence of acetate buffer. The second method was the reaction of the sodium arylsulfinates with preliminarily prepared 3-bromo-2-butenenitrile in the same condition. The resulting compounds - β-cyanovinylsulfones were characterized by spectral methods.

Key words: arylsulfinates; 3-arylsulfonyl-2-butennitriles; 3-bromo-2-butenenitrile; 2,3-dibromobutanenitrile; β-cyanovinylsulfones.

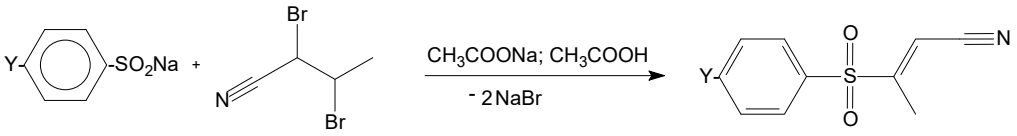
Introduction

In our previous reports [2-4], the general possibility of synthesizing γ-functionalized allylsulfones was discussed. The synthesis of various α-cyanovinylsulfones were published [1,6,7], but no evidence for the synthesis of β-cyanovinylsulfones. Their synthesis represents an interesting endeavour not only by the presence of multiple reactive centers in them, but also by the ability to synthesis new compounds with potential biological activity.

In the present work, we propose synthesis of β-cyanovinylsulfones, according to two separate and independent methods. In the first case (**Scheme 1**) this synthesis was implemented by

employing arylsulfinates (**1a-c**) and 2,3-dibromobutanenitrile (**2**) as starting materials, whereas, in the second (**Scheme 2**), the compound (**1a-c**) and 3-bromo-2-butenenitrile (**3**) were used as starting materials.

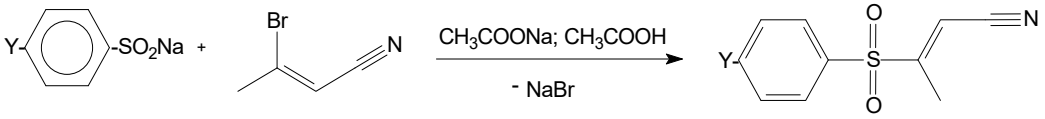
Scheme 1



(1a-c) (2) (4a-c)
E+Z

Y = H, CH_3, NO_2

Scheme 2



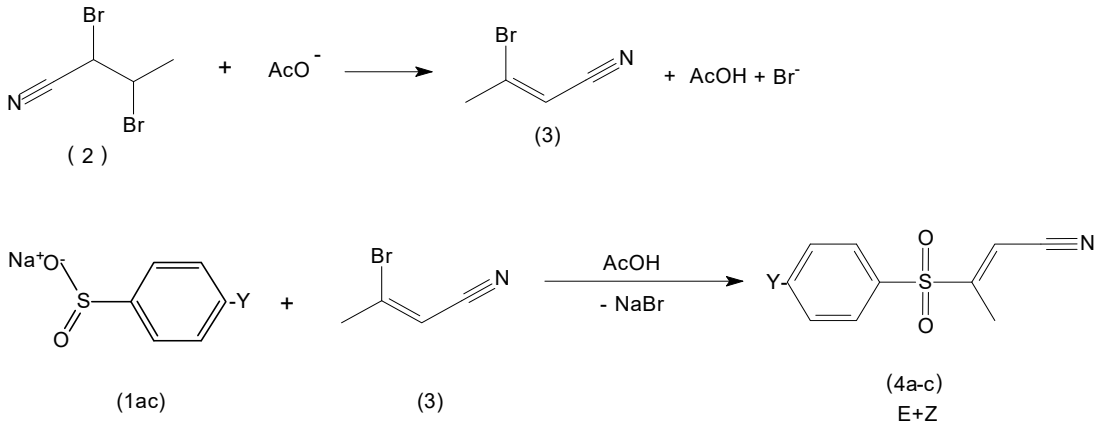
(1a-c) (3) (4a-c)
E+Z

Y = H, CH_3, NO_2

Result and discussion

The structural prerequisite for the successful course of reaction, according to scheme 1 is the strongly pronounced proton acidity of the α-H-atom in 2,3-dibromobutanenitrile affected by the presence of the cyano group, brome substituent and acetate anion. The deprotonation of 2,3-dibromobutanenitrile causes spontaneous release of bromide anion, resulting in the formation of 3-bromo-2-butenenitrile. The latter reacts with the sodium arylsulfinates, forming 3-arylsulfonyl-2-butenenitriles. Therefore, the probable course of the reaction, represented in accordance with scheme 1 is as follows:

Scheme 3



An indirect evidence for this kind of reaction proceeding is the parallel method (**Method B**) for the preparation of (**4a-c)** designed by us. According to this method, 3-bromo-2-butenenitrile was preliminarily synthesized by dehydrobromination of 3,4-dibromobutanenitrile under heating with ethanol solution of AcONa.

The scheme 1 reaction was implemented in water/alcohol medium and acetate buffer. The reaction mixture was heated in an ampoule for eight hours at 70^{o}C. The corresponding yields of (**4a-c)** for this method were within 63 to 72 %.

The scheme 2 reaction (method B), occurring also in water/alcohol medium and acetate buffer was conducted at the same condition and corresponding yields of (**4a-c)** for this method were 64 – 88 %. Table 1 gives the yields of (**4a-c)** obtained by employing methods A and B respectively.

Table1. Yields and E/Z ratio of the β-cyanovinylsulfones 4a-c

№	Y	Name	M_M	Yield, methods,(%)		E/Z, %
				A	B	
4a	H	3-Phenylsulfonyl-2-butenenitrile	207.25	76	64	44/56
4b	CH_3	3-(4-Toluenesulfonyl)-2-butenenitrile	221.27	74	88	55/45
4c	NO_2	3-(4-nitrobenzenesulfonyl)-2-butenenitrile	252.24	63	76	56/44

We found out in the course of the present study, that the optimum ratio of the reactants for all methods used was 1:1.

The compounds of the type **4a-c** are crystalline solids, which were soluble in 1,4-dioxane and acetone, however, they did not dissolve in water and n-hexane. These compounds showed good stability on prolonged storage and melted without decomposition. Their structures were examined by using spectral methods as well as elemental and TGA analyses.

IR spectra of **4a-c** indicated strong bands, characteristic for asymmetric and symmetric stretching vibrations of sulfonyl group (1300 - 1145 cm^{-1}). Absorption bands for C–H stretching vibrations in an aromatic ring were observed within 3100 - 3000 cm^{-1}. Skeletal absorption bands within 1620 - 1440 cm^{-1} for aromatic nucleus were also observed. Stretching vibrations of CN-group observed at 2220cm^{-1}. For **4b** and **4c** samples, deformation C–H vibrations from 850 - 800 cm^{-1} were detected, which indicated the presence of *p*-disubstituted benzene ring. The presence of methyl group for **4b** in the benzene ring was proved by the stretching asymmetric and symmetric vibrations at 2920 cm^{-1}. The characteristic absorption bands for the C=CH group at, approximately, 3070, 3040, 1615, 775 cm^{-1} as well as for vinyl group at 3020 cm^{-1} were also detected. The presence of conjugated CH=CH group for all samples was proved by the stretching

vibrations at 1630 - 1590 cm^{-1}. Strong characteristic C–S absorption at 1080 cm^{-1} was also observed for the samples studied. The symmetric and asymmetric stretching vibrations for NO_2 group in **4c** corresponded to the strong bands at 1520 и 1310 cm^{-1}.

The spectral methods data indicated that the final products 4a-c represented mixtures of E/Z stereoisomers. We were unable to separate the latter by column chromatography (silica L100/250-Chemapol). The ratios of these isomers given in the experimental part were associated with the products obtained by method B.

Experimental

Melting points were measured on an derivatograph OD-102 (uncorrected). Elemental analyses were performed, using a Series-4 instrument (Perkin-Elmer) and a programmable multiwavelength detector. UV spectra were recorded on Specord UV-VIS. IR spectra were recorded on a Specord 75 IR spectromerter. ^1H spectra were measured with a BRUKER DRN-500 ADVANCE spectrometer at 250 MHz.

The compounds of the **1a-c** type were prepared before commencing the reaction by employing equimolar ratios of arylsulfinic acids, prepared by known method [5] and NaOH.

Preparation of 2,3- dibromobutanenitrile (2). 0.01 mol 3-butenenitrile, dissolved in 200 ml of chloroform (previously dried with magnesium sulphate) were placed into four necked round bottom flask equipped with a thermometer, stirrer and reflux and was heated to 45-50^oC. In a dropping funnel was poured 0.012 mol of bromine dissolved in 700 ml of chloroform and added slowly dropwise to a gently refluxing mixture. After addition of the entire amount of bromine solution, the reaction mixture was stirred for a further 1 hour and solvent was distilled under

vacuum. The resulting product distilled almost completely in a fraction with n^{d}_{20} = 1,529, b.p.86ºC and yield 94%.

Preparation of 3-bromo-2-butenenitrile (3). In a three-necked flask equipped with a stirrer and thermometer was charged with a solution of 0.01 mol of 2,3-dibromobutanenitrile in 100 ml of ethanol. Then 0,011 mol CH3COOK was added in the flack. The reaction mixture was heated to reflux, cooled, and the precipitated NaBr was filtered. The filtrate was poured into water. After extraction with ether the ethereal extracts were dried with $MgSO_4$. The ether was evaporated and the residue was subjected to vacuum distillation. Prepared slightly yellowish liquid has lacrimal properties and it is soluble in benzene, alcohol, dioxane, chloroform. The yield reaches 80%, n^{d}_{16} = 1,489, b.p 42-43ºC /5 mm Hg.

General procedure for the preparation of vinylsulfones 4a-c, according to method A:

0.001 mol acetic acid and 0.001 mol sodium acetate were added to the 0.001 mol sodium-4-arylsulfinate solution (1), prepared from equimolar ratios of arylsulfinic acid and NaOH in 10 ml distilled water prior to commencing the reaction. Following the dissolution of reactants, freshly prepared solution of 0.001 mol 2,4-dibromobutanenitrile (2) in 10 ml ethanol was also added. The starting reaction mixture transferred into an ampoule and was left to react for 8 h at 70ºC. The mixture was then poured into distilled water and left to stay overnight. The crystals obtained were separated by filtration and, subsequently, purified by re-crystallization.

General procedure for the preparation of vinylsulfones 4a-c, according to method B

To the solution of 0.001 mol sodium arylsulfinate in 10 ml distilled water, 0.001 mol acetic acid and freshly prepared solution of 0.001 mol 3-bromo-2-butenenitrile (3) in 10 ml ethanol was added. The reaction mixture was left to stay for 3 – 4 days at room temperature. The starting

reaction mixture transferred into an ampoule and was left to react for 8 h at 70ºC. The mixture was then poured into distilled water and left to stay overnight. The crystals obtained were separated by filtration and, subsequently, purified by re-crystallization.

3-phenylsulfonyl-2-butenenitrile (4a) - White crystals, m.p.=95ºC(toluene/hexane); **IR** (KBr) 3070, 3040, 2980, 2910, 2220, 1625, 1580, 1475, 1390, 1310, 1230, 1140, 1185, 1165, 1080, 1000, 980, 900, 810, 740, 580, 535 cm^{-1}; **H^1-ЯМР**($CDCl_3$) δ_H ppm, 2,17-2,18 (s, 3H, -$C(CH_3)$=CH), 6,483-6,489 (s, 1H, = CH-CN), 7.53-7.59(m, 2H, ArH), 7.64-7.67(m, 1H, ArH), 7.74-7.73(m,2H, ArH); **Calcd**: C=57.96, H=4.38, N=6.76, O=15.44, S=15.47; **Found**:C=57.96, H=4.39, N=6.74, O=15.43, S=15.48

3-(4-toluenesulfonyl)-2-butennitrile (4b)- White crystals, m.p.=95ºC(toluene/hexane); **IR** (KBr) 3060, 2980, 2920, 2220, 1630, 1600, 1400, 1320, 1290, 1230, 1180, 1140, 1080, 975, 900, 815, 720, 630, 590, 560, 510 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ_H ppm, 2,15 (s, 3H, -$C(CH_3)$=CH), 2.41(s, 3H, CH_3). 6.42-6.44(m, 1H, =CH-CN), 7.26-7.39(m, 2H, ArH), 7.69-7.78(m,2H, ArH); **Calcd**:: C=59.71, H=5.01, N=6.33, O=14.46, S=14.49; **Found**: C=59.70, H=4.38, N=6.75, O=15.45, S=15.47

3-(4-nitrobenzenesulfonyl)-2-butenenitrile (4c)- Canary crystals, m.p.=167ºC (dioxane/ toluene); **IR** (Kbr) 3100, 3070, 3020, 3000,2980, 2920, 2220, 1630, 1520, 1440, 1350, 1310, 1230, 1180, 1145, 1135, 1080, 980, 900, 850, 750, 730, 700, 685, 580, 550, 460, 430 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ_H ppm, 2,15 (s, 3H, -$C(CH_3)$=CH), 2.41(s, 3H, CH_3). 6.42-6.44(m, 1H, =CH-CN), 8.08-8.13(m, 2H, ArH), 8.35-8.40(m, 2H, ArH); **Calcd**: C=47.61, H=3.20, N=11.11, O=25.37, S=12.71; **Found**: C=47.58, H=3.21, N=11.09, O=25.38, S=12.74

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