SYNTHESIS AND REACTIONS OF 2-CHLOROVINYL SULFONES

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Methods for the preparation of unsubstituted (*E*)-2-chlorovinyl sulfones are reviewed. Literature data on substitution of chlorine atom in 2-chlorovinyl sulfones leading to formation of different types of disubstituted ethenes are presented also. Synthesis of novel heterocyclic compounds directly from 2-chlorovinyl sulfones is also included in the present review.

Key words: 2-chlorovinyl sulfones, addition, radical 2-chlorovinylation, heterocycles

INTRODUCTION

Functionalized unsaturated sulfur-containing compounds are investigated widely as valuable intermediates in organic synthesis [1–3]. 2-Chlorovinyl sulfones, among them sulfur-containing compounds, are extensively investigated during last years. For example, 2-chlorovinyl sulfones exhibit high cytotoxic, antimicrobial [4], fungicidal [5] activities and are used in veterinary medicine and cosmetic compositions [6].

Synthesis and reactions of 2-chlorovinyl sulfones aren't reviewed till now and therefore is an aim of the present work. Transformations of different types of organic compounds bearing unsubstituted 2-chlorovinylsulfonyl group are included in this work.

SYNTHESIS OF 2-CHLOROVINYL SULFONES

2-Chlorovinyl sulfones are typically prepared by oxidation of 2-chlorovinyl sulfides [7] with H_2O_2 in AcOH [8, 9], H_2O_2 / AcOH / H_2SO_4 [10, 11] H_2O_2 / AcOH / Ac_2O [12] or *m*-chloroperbenzoic acid (*m*-CPBA) in CH_2Cl_2 [13]. We have recently described new and simple two-step method for the synthesis of 2-chlorovinyl sulfones **3** by oxidation of the corresponding 2-chlorovinyl sulfides **2**, prepared by phase transfer catalytic alkylation of thiols **1** in the system *solid KI* / *solid K₂CO₃* (then *solid KOH*) / 18-crown-6 / *PhMe* [14, 15].

(*E*)-2-Chloroethenylphenyl sulfone (**5**) was prepared from benzenesulfanyl chloride **4** on treatment with acetylene and then oxidation with *m*-CPBA [11, 16]. Isomer (*Z*) of compound **5** was easily obtained by decarboxylative chlorination of (*Z*)-3-(phenylsulfanyl)acrylic acid **6** followed by oxidation with H₂O₂. Similarly acid *E*-**6** afforded stereoselectively *E*-isomer of 2-chlorovinyl sulfone **5** [10].

Two methods for the preparation of 2-chlorovinyl sulfones from the corresponding disulfides were presented in literature [12, 17]. Thus, treatment of disulfide **7** with chlorine in CCl₄ at room temperature and then with ethyl acetate leads to formation of vinyl derivative **8**. Oxidation of compound with *m*-CPBA in CH₂Cl₂ afforded *E*-isomer of chlorovinyl sulfone **9**. Sulfuryl chloride as chlorinating agent of disulfides was also used in the synthesis of (*E*)-2-chlorovinyl sulfones [17].

Some methods of synthesis of 2-chlorovinyl sulfones from different sulfones or sulfonyl chlorides were presented. Thus, treatment of 2,2-dichloroethanesulfonylarenes with Et₃N [18, 19], Et₃N / PhH [20-22] or Et₃N / CH₂Cl₂ [23] selectively leads to formation only of *E*-isomers of 2-chlorovinyl sulfones. For example, reaction of 2,2-dichloroethanesulfonylbenzene (**10**) with Et₃N in mixture of diethyl ether and dichloromethane at 15 °C afforded product (*E*)-**5** in 97% yield [24].

Treatment of benzene sulfonyl chloride (**11**) with naphthalene-1,4-diylamine hydrochloride in the presence of AlCl_3 in chloroform and then with Et_3N afforded (*E*)-**5** in 78% yield [21]. Interestingly, that treatment of ethynyl *p*-tolyl sulfone (**12**) with ethylaluminum dichloride in benzene leads to aluminated intermediate **13**. Quenching the reaction mixture with D_2O afforded deuterated product **14** in 58% yield [25].

Some works were dedicated to synthesis of nitro [26], amino [27] and diazo [28] derivatives of 2-chlorovinyl sulfones. For example, reaction of amino derivative of sulfone **15** with NaNO_2 in concentrated HCl and treatment of reaction mixture with *N*-methyl-4-hydroxy-2-quinolone (**16**) and NaOH afforded diazo derivative of 2-chlorovinyl sulfone (**17**) [28].

Finally, isomerization of *Z*-isomer of *p*-nitrophenyl 2-chlorovinyl sulfone to the corresponding *E*-isomer readily proceeded in aqueous nitric acid in the presence of NaNO_2 [10].

REACTIONS OF 2-CHLOROVINYL SULFONES

Substitution of chlorine atom in 2-chlorovinyl sulfones

Chlorine atom in 2-chlorovinyl sulfones was readily substituted by iodine atom [23] or hydroxyl group. Thus, treatment of compound (*E*)-**5** with an excess of NaI in acetone at 130°C afforded the corresponding iodo derivative **18** in

76% yield. Reaction of 2-chlorovinyl sulfone **19** with aqueous NaOH lead to 2-hydroxyvinyl sulfone **20** [19].

Some works were dedicated to conjugate addition of O-nucleophiles to 2-chlorovinyl sulfones. The interaction of 2-chlorovinyl sulfones with sodium methylate is strongly influenced by amounts of this base. Generally, interaction of compounds **21** with NaOMe in MeOH leads to formation of mixture of mono- **22** and double addition products **23** [29]. Interaction of 2-chlorovinyl sulfone **5** with MeOH, and then with BuLi / MeI afforded (E)-2-methoxy-1-methyl-1-(phenylsulfonyl)ethylene (**24**) [30].

Addition of different carboxylic acid derivatives to 2-chlorovinyl sulfone **9** was investigated in details in article [17]. It is interesting, that addition of 4,4-dimethyl-3-hydroxypentanoic acid to compound **9** afforded only carboxylic group addition product **25**.

Addition of different N-nucleophiles (primary and secondary amines) to 2-chlorovinyl sulfones readily proceeded in MeOH [31], EtOH [31, 32], DMF [17], MeCN [33] and in the system Cs_2CO_3 / 18-crown-6 / PhMe [34]. Interaction of 2-chlorovinyl sulfone **5** with hydroxylamine in the mixture EtOH / H_2O afforded hydroxylamine **26**. Similarly hydrazine **27** [32] and azide **29** [35] derivatives were prepared from the corresponding chlorovinyl sulfones **9** and **28**, correspondingly. 2-Chlorovinyl sulfones react also with tertiary amines forming the corresponding ammonium salts [33].

Some articles were dedicated to addition of S- and Se-nucleophiles to 2-chlorovinyl sulfones. Thus, 2-mercaptoacetic acid undergoes addition to 2-chlorovinyl sulfone **5** in the presence of NaOH in EtOH. (E)-Phenylsulfonyl-ethenemercaptoacetic acid (**30**) was isolated in 72% yield [36]. Reaction of 2-chlorovinyl sulfones **31** with Na_2S in dioxane [37] or MeOH [38] afforded sulfides **32** in yields up to 90%. Sulfinic acids and 2-chlorovinyl sulfones in the presence of NaHCO_3 [32] or salts of sulfinic acids in MeOH [20] also gave the corresponding addition products. Phenylselenol was successfully added to 2-chlorovinyl sulfones in the presence of Et_3N / PhH [39], Et_3N / PhMe [34] and Cs_2CO_3 / 18-crown-6 / PhMe [34].

Suzuki reaction of 2-chlorovinyl sulfones with aromatic and heteroaromatic boronic acids was investigated [14]. The catalytic system 2-chlorovinyl derivative **5** or **34** / $\text{ArB}(\text{OH})_2$ / solid K_3PO_4 / $\text{PdCl}_2(\text{dppf}) \cdot \text{CH}_2\text{Cl}_2$ in the molar ratio of 1 : 1.5 : 2 : 0.04 was used as the most efficient one for the synthesis of products **33** and **35**. The formation of arenes or hetarenes and homocoupling products of boronic acids (Ar-Ar) as minor products was also observed.

Interaction of chlorovinyl sulfones **36** with active methylene compounds (such as diethyl malonate or diethyl acetamidomalonate) in the presence of NaH leads to formation of the addition products **37** in 13–30% yields [40]. Experiments show, that the catalytic system solid Cs_2CO_3 / 18-crown-6 / CH_2Cl_2 was non-effective in the reaction of addition of active methylene compounds to chlorovinyl sulfone **38** (Method A). Under these conditions the desired products were isolated only in yields up to 9%. The synthesis of desired products **39** was carried out using triethylamine-catalyzed synthesis, too (Method B). Using triethylamine method, alkenes **39** were isolated in yields up to 87%.

Finally, Takai-Hiyama-Nozaki-Kishi reaction of 2-chlorovinyl sulfones **40** with aldehydes in the system CrCl_2 / NiCl_2 / THF at room temperature afforded unsaturated sulfones **41** in 17-96% yields [41].

Radical 2-chlorovinylation

Radical chlorovinylation of different alkyl iodides (for example, substrates **42** and **43**) with (*E*)-1-chloro-2-ethanesulfonylene (44) in the presence of lauroyl peroxide afforded the products **45** and **46**, correspondingly [42].

Synthesis of heterocycles from 2-chlorovinylsulfones

Synthesis of 2,3-dihydrofuran derivatives from 2-chlorovinyl sulfones was described in some articles [18, 24, 30, 43, 44]. Thus, interaction of epoxy alcohol **47** with chlorovinyl sulfone **5** afforded intermediate ether **48**. Treatment of this product with lithium hexamethyldisilylamide (LiHMDS) in THF afforded dihydrofuran derivative **49** in 60% yield [44].

Novel method of synthesis of 1,3-dithiolanes and 1,3-dithianes **51** was elaborated [45]. Reaction of 2-chlorovinyl sulfones **50** with 1,2-ethanedithiol or 1,3-propanedithiol in the system Et₃N/ PhMe at 80 °C leads to formation of the desired products **51**. Treatment of 2-chlorovinyl sulfone **5** with ethylene glycol in the presence of NaH in THF leads to 2-benzenesulfonylmethyl[1,3]dioxolane (**52**) [46].

Treatment of chlorovinyl sulfone **5** with epoxy alcohol **53** in the presence of NaH / THF, followed by cyclization of an intermediate with lithium diisopropylamide (LDA) gives pyran **54** [18].

1,2,3,4,4a,5-Hexahydropyrazino[2,1c][1,4]benzothiazine-6,6-dioxide (**56**) was obtained from 2-chlorovinyl sulfone **55** and ethane-1,2-diamine in monoethylene glycol ethyl ether [47]. Finally, polycyclic oxepine derivative **57** was obtained from 2-chlorovinyl sulfone **5** and (*R*)-2,2'-dihydroxy-1,1'-binaphthyl in the presence of NaH in THF [46].

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2-HLORVINILSULFONU SINTĒZE UN REAKCIJAS

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K O P S A V I L K U M S

Apkopotati dati par 2-hlorvinilsulfonu sintēzi un reakcijām. Apskata pirmajā nodaļā apkopotas 2-hlorvinilsulfonu sintēzes metodes izmantojot, oksidēšanas un eliminēšanas reakcijas. Tālākajā darbā apkopotas 2-hlorvinilsulfonu reakcijas ar dažādiem nukleofiliem reaģentiem, kā arī jaunu heterociklisko savienojumu sintēze no 2-hlorvinilsulfoniem.

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