# EXCHANGE OF THE AMINO GROUP IN β-AMINO DERIVATIVES OF SULFOLANE

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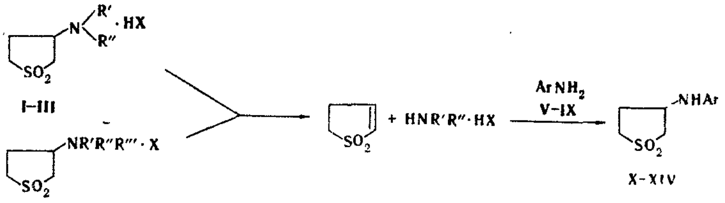
The lability of the C–N bond in a number of β-amino derivatives of sulfolane was investigated. Alkyl–aryl transamination and a number of reactions of salts of aminosulfolanes with nucleophilic reagents were realized.

The amino group in β-amino ketones [1], β-amino acids [2], and β-aminonitriles [3] has the capacity to undergo substitution caused by elimination of amine and formation of the corresponding olefin. Elimination is not observed in β-piperidinoethyl phenyl sulfone [4], although the hydrochloride and methiodide react quantitatively with thiophenols via an elimination–addition mechanism [5]. In the present research we have investigated the capacity of the amino group of some β-amino derivatives of sulfolane to undergo substitution. We have previously described [6] cases involving exchange of the alkoxy group. It seemed of interest to study the lability of the C–N bond for comparison of the properties of β-heteroatom substituted sulfolanes and for elucidation of the possibilities of the practical utilization of accessible amino derivatives for the preparation of various sulfolane derivatives in place of the difficult-to-obtain 2-sulfolene.

We have found that primary, secondary, and tertiary β-alkylaminosulfolanes are resistant to thermal action and nucleophilic exchange. Heating of 3-N-methylaminosulfolane (IIa) and 3-N-dimethylaminosulfolane (IIIa) at 170–175°C for 7 h leads to partial resinification and the formation of a very small amount of 2-sulfolene, the presence of which was established by thin-layer chromatography (TLC) on aluminum oxide. The C–N bond in hydrochlorides Ib–IIIb and sulfolanyltetramethylammonium iodide (IV) is appreciably weakened, and the amino group is readily cleaved to give 2-sulfolene. Considering this, we attempted to combine the elimination of β-aminosulfolane salts to 2-sulfolene with addition of arylamines to it. The corresponding arylaminosulfolanes (X-XIV), which were identical to those previously described [7], were obtained by heating hydrochlorides Ib–IIIb and IV with arylamines V–IX at 170–175° and a molar ratio of 1 : 2. The influence of steric and inductive effects of the substituents of arylamines V–IX in alkyl–aryl transamination and addition of arylamines to 2-sulfolene [7] is apparently similar. The presence of 2-sulfolene in the products of the alkyl-aryl transamination reaction makes it possible to assume that the process occurs via a cleavage –



Ia $R'=R''=H$; Iб $R'=R''=H$; $X=Cl$; IIa $R'=CH_3$, $R''=H$; IIb $R'=CH_3$, $R''=H$, $X=Cl$; IIIa $R'=R''=CH_3$; IIIb $R'=R''=CH_3$, $X=Cl$; IV $R'=R''=R'''=CH_3$; $X=I$; V, X $Ar=C_6H_5$; VI, XI $Ar=p\text{-}Cl=C_6H_4$; VII, XII $Ar=p\text{-}CH_3C_6H_4$; VIII, XIII $Ar=m\text{-}CH_3C_6H_4$; IX, XIV $Ar=o\text{-}CH_2C_6H_4$.

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addition scheme. Inasmuch as hydrochloride Ib is more accessible than 2-sulfolene, the reaction under consideration is of practical interest as a method for the synthesis of arylaminosulfolanes [8].

The results of alkylation of methiodide IV by means of the sodium derivative of malonic acid and the reaction of I-IV with alkoxides and mercaptides can also be explained by cleavage–addition. The high yields of the diamide (XV) and diethyl ester (XVI) of 3-sulfolanylmalonic acid are in agreement with the increased (as compared with $C_2H_5O^-$) nucleophilicity of $^-$CHXV carbanions in nucleophilic addition reactions [9]. The decrease in the yields of the products of alcoholysis with n-butanol (XVII) and of mercaptolysis with n-butylmercaptan (XIX) in the order IV > IIIb-Ib > IIIa-Ia corresponds to the known lability of the C–N bond in such compounds [1-5]. An effect of the alcohol structure that is similar to the addition in [10] was established in the reaction of IV with isomeric n-, sec-, and tert-butyl alcohols. The corresponding butoxysulfolanes (XVII-XVIII) were identified by TLC. 3-Cyanosulfolane (XX), 3-mercaptosulfolane, which was isolated as sulfolane-3-sulfonyl chloride (XXI), the sodium salt of sulfolane-3-sulfonic acid (XXII), and 3-sulfolanyl phenyl sulfone (XXIII), respectively, were obtained by heating IV with aqueous solutions of potassium cyanide, potassium sulfide, potassium sulfite, and sodium benzenesulfinate. The products were identified from the IR spectra and mixed-melting-point determinations with compounds synthesized by reaction with 2-sulfolene.

## EXPERIMENTAL

Starting compounds I-IV were obtained by the methods presented in [11]. Chromatography was carried out in a thin layer of activity II aluminum oxide by elution with diethyl ether and development with iodine vapors.

3-Phenylaminosulfolane (X). A mixture of 1.9 g (0.01 mole) of IIb and 4.9 g (0.02 mole) of aniline was heated at 175° for 6 h. The reaction mixture was then cooled and treated successively with ether and chloroform. The solid material (0.7 g) was methylamine hydrochloride. The solvents were removed from the ether and chloroform extracts to give 1.3 g (60%) of X with mp 118-119° (from 20% aqueous ethanol). The yield of X in the reaction of V with Ib was 54%, while the yields with IIIb and IV were 60% and 58%, respectively.

Products XI-XIV were similarly obtained by reaction of IIIb with VI-IX. The yields of XI-XIII were, respectively, 25, 71, 70%, and the melting points were 123-124, 124-125, and 90-92°. Product XIV was not isolated [7].

3-Sulfolanylmalonic Acid Diamide (XV). A 0.46-g (0.02 mole) sample of sodium was dissolved in 10 ml of absolute ethanol, 2.0 g (0.02 mole) of malonic acid diamide and 6.0 g (0.02 mole) of IV were added, and the mixture was heated at 60° for 8 h. The reaction mixture was cooled and neutralized with hydrochloric acid. The resulting precipitate was removed by filtration, washed with 2-3 ml of ice water, and recrystallized from 40% aqueous ethanol to give 3.5 g (80%) of XV with mp 268-270° [12]. Diethyl 3-sulfolanylmalonate (XVI) was similarly obtained. The yield of product with mp 61-63° (from ethanol) was 60% [12].

3-n-Butoxysulfolane (XVII). A 0.2-g (0.01 g-atom) sample of sodium was dissolved in 17 ml (0.1 mole) of n-butanol, 3.3 g (0.02 mole) of IIIa was added, and the mixture was heated at 65-70° for 10 h. The excess n-butanol was removed, and the residue was dissolved in ether. Hydrogen chloride was passed through the ether solution, and the precipitated IIIb was removed by filtration and washed with ether. The ether extract was evaporated to give 0.6 g (15%) of XVII, which was identified by TLC ($R_f$ 0.56). The reactions of n-butanol with Ia and IIa were carried out under the same conditions. Product XVII was detected by TLC. The reaction of IV with n-butanol gave XVII (92%), and the reaction of IV with sec-butanol gave XVIII (64%) ($R_f$ 0.54); resinification of the mixture, in which 2-sulfolene was detected by TLC, was observed with tert-butanol.

3-Sulfolanyl Butyl Sulfide (XIX). A 0.3-g (0.012 g-atom) sample of sodium was dissolved in 10 ml (0.1 mole) of butyl mercaptan, 3.0 g (0.01 mole) of IV was added, and the mixture was heated at 65° for 10 h. The excess butyl mercaptan was removed. The residue was washed with 3 ml of water and dried to give 2.0 g (96%) of XIX. The product was oxidized with hydrogen peroxide in acetic acid to 3-sulfolanyl butyl sulfone, which was identified by a mixed-melting-point determination with the compound obtained by the method in [13]. Sulfide XIX was obtained under the conditions used to obtain XVII by reaction of n-butyl mercaptan with IIIa (18% yield); XIX was detected only by TLC ($R_f$ 0.45) in the reaction with Ia and IIa.

3-Cyanosulfolane (XX). A solution of 3.0 g (0.01 mole) of IV and 0.9 g (0.014 mole) of potassium cyanide in 3 ml of water was heated at 55-60° for 10 h. The water was evaporated, and the dry residue was extracted with chloroform–dioxane (1 : 1). The solvent was removed from the extract to give 0.5 g (41%) of 3-cyanosulfolane with mp 118-119° (from ethanol) [14].

Sulfolane-3-sulfonyl Chloride (XXI). A mixture of 3.0 g (0.01 mole) of IV, 10.0 g of a 25% solution of sodium hydrosulfide, and 5 ml of water was heated at 60° for 10 h. Chlorine was passed through the cooled solution while maintaining the temperature at 30-40°. The resulting precipitate was crystallized from acetone to give 0.5 g (22%) of sulfolane-3-sulfonyl chloride with mp 117-118° [15].

Sodium Sulfolane-3-Sulfonate (XXII). A solution of 3.0 g (0.01 mole) of IV and 1.3 g (0.01 mole) of sodium sulfite in 3 ml of water was heated at 60° for 10 h, after which the water was evaporated. The residue was recrystallized from 40% aqueous methanol to give 1.8 g (81%) of sodium sulfolane-3-sulfonate. Found %: S 31.2. $C_4H_7O_5O_5S_2Na$. Calculated %: S 31.1.

3-Sulfolanyl Phenyl Sulfone (XXIII). Similarly, 1.6 g (60%) of 3-sulfolanyl phenyl sulfone with mp 158-160° (from methanol) [16] was obtained from 3.0 g (0.01 mole) of IV and 1.8 g (0.011 mole) of sodium benzenesulfinate.

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