FUNCTIONAL DERIVATIVES OF THIOPHENE

XVI.* TOSYLAMINOTHIOPHENES

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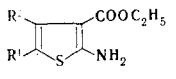
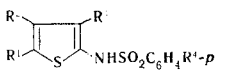
5-Tosylamino-2,3-dialkylthiophenes, which are alkylated to the corresponding 5-alkyl(tosyl)-amino derivatives, were synthesized from 2-amino-3-carbethoxy-4,5-dialkylthiophenes by tosylation and subsequent decarboxylation.

We obtained tosyl and p-nitrophenylsulfonylamino derivatives of thiophene III-VII by reaction of 2-amino-3-carbethoxythiophenes I and II with arenesulfonyl chlorides. Selective alkaline hydrolysis of esters III and IV leads to tosylaminothiophenecarboxylic acids VIII and IX. The latter are converted to tosylaminothiophenes with a free β position when they are heated above their melting points.

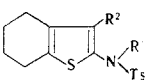
The action of alkali on the tosylaminothiophenes readily gives the N-sodio derivatives, which we were able to alkylate with dialkylaminoalkyl chlorides, ethylene chlorohydrin, and β-chloropropionic acid. Hydroxyethyl derivative XV reacts with thionyl chloride to give chloroethyl derivative XVII. Thiophene X was thiocyanated by the method in [2]. The reduction of p-nitro derivative V leads to sulfanilamide VII.



I, II



III–XI



XII–XVIII

I $R^1R^2=(CH_2)_4$; II $R^1=R^2=CH_3$; III $R^1R^2=(CH_2)_4$, $R^3=COOC_2H_5$, $R^4=CH_3$; IV $R^1=R^2=R^4=CH_3$, $R^3=COOC_2H_5$; V $R^1R^2=(CH_2)_4$, $R^3=COOC_2H_5$, $R^4=NO_2$; VI $R^1=R^2=CH_3$, $R^3=COOC_2H_5$, $R^4=NO_2$; VII $R^1R^2=(CH_2)_4$, $R^3=COOC_2H_5$, $R^4=NH_2$; VIII $R^1R^2=(CH_2)_4$, $R^3=COOH$, $R^4=CH_3$; IX $R^1=R^2=R^4=CH_3$, $R^3=COOH$; X $R^1R^2=(CH_2)_4$, $R^3=H$, $R^4=CH_3$; XI $R^1=R^2=R^4=CH_3$, $R^3=H$; XII $R^1=Na$, $R^2=H$; XIII $R^1=CH_2CH_2N(C_2H_5)_2\cdot HCl$, $R^2=H$; XIV $R^1=-(CH_2)_3N(CH_3)_2\cdot HCl$, $R^2=H$; XV $R^1=-CH_2CH_2OH$, $R^2=H$; XVI $R^1=CH_2CH_2COOH$, $R^2=H$; XVII $R^1=CH_2CH_2Cl$, $R^2=H$; XVIII $R^1=H$, $R^2=SCN$

EXPERIMENTAL

5-Phenylsulfonylamino-4-carbethoxy-2,3-dialkylthiophenes (III-VI). Pyridine (20 ml) was added to 0.1 mole of amine I or II in 30 ml of dry dichloroethane, and the mixture was allowed to stand at room temperature for 15 min. The arenesulfonyl chloride (0.11 mole) was then added in portions with stirring, and the mixture was refluxed on a water bath for 4 h. It was then cooled, acidified with dilute hydrochloric acid, and refluxed for 1 h. It was then allowed to stand at room temperature overnight, and the resulting precipitate was removed by filtration. The filtrate was extracted with dichloroethane, the dichloroethane was removed by distillation almost to dryness, and the solid material was removed by filtration. Both precipitates were combined and washed with methanol. Data on III and V-VI are presented in Table 1. Compound IV had mp 91.5-92.5° (from methanol) (mp 91-93° [3]).

5-(p-Aminophenylsulfonylamino)-4-carbethoxy-2,3-tetramethylthiophene (VII). A 1.7-g sample of iron filings was added to a solution of 2.05 g (0.005 mole) of nitro compound V in 160 ml of 65% aqueous dioxane, and a solution of 0.1 ml of hydrochloric acid in 2 ml of water was added dropwise with stirring at 70-80°. The mixture was refluxed for 6 h, after which it was filtered to remove the sediment. Activated charcoal was added

*See [1] for communication XV.

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TABLE 1. Tosylaminothiophenes*

Compound	mp, °C†	Empirical formula	Yield, %
III	124—125	$C_{18}H_{21}NO_4S_2$	88
V	139—140	$C_{17}H_{18}N_2O_6S_2$	44
VI	127,5—128	$C_{15}H_{16}N_2O_6S_2$	25
VIII	190—191	$C_{16}H_{17}NO_4S_2$	90
IX	188—189	$C_{14}H_{15}NO_4S_2$	74
X	138—139	$C_{15}H_{17}NO_2S_2$	72
XI	129—130	$C_{13}H_{16}NO_2S_2$	43,2
XIII	156—157	$C_{21}H_{30}N_2O_2S_2 \cdot HCl$	41,8
XIV	184—185	$C_{20}H_{28}N_2O_2S_2 \cdot HCl$	52,2

*The results of elementary analysis for C, H, N, and S are in agreement with the calculated values.
†The substances were recrystallized: III, V, VI, VIII, and IX-XI from methanol, and XIII and XIV from acetone—ether).

to the filtrate, the mixture was refluxed for a few minutes, and the charcoal was removed by filtration. The solvent was removed by vacuum distillation, and the residue was recrystallized from methanol to give 1.06 g (55.7%) of a product with mp 171-172° (from methanol). Found: C 53.5; H 5.3%. $C_{17}H_{20}N_2O_4S_2$. Calculated: C 53.7; H 5.3%.

5-Tosylamino-2,3-dialkylthiophene-4-carboxylic Acids (VIII, IX). A solution of 2.4 mole of sodium hydroxide in 650 ml of water was added to a solution of 0.6 mole of esters III or IV in a mixture of 240 ml of methanol and 650 ml of dioxane, and the mixture was refluxed on a water bath for 5 h. It was then poured into water, and the aqueous mixture was acidified with dilute hydrochloric acid. The precipitate was removed by filtration and recrystallized from methanol—dioxane—water. Data on VIII and IX are presented in Table 1.

5-Tosylamino-2,3-dialkylthiophenes (X, XI). Acid VIII or IX was heated on a Wood's metal bath at 200-210° for 7-10 min, after which it was cooled and recrystallized from methanol. Data on X and XI are presented in Table 1.

Preparation of Sodium Derivative XII. A solution of 0.167 mole of sodium hydroxide in 75 ml of methanol was added to a solution of 0.167 mole of X in 75 ml of acetone, after which the solvents were removed by distillation to dryness on a water bath. Sodium derivative XII was used for alkylation without additional purification.

5-Diethylaminoethyl(tosyl)amino-2,3-tetramethylenethiophene Hydrochloride (XIII) and 5-Dimethylaminopropyl(tosyl)amino-2,3-tetramethylenethiophene Hydrochloride (XIV). A reaction mixture consisting of 0.02 mole of XII, 0.022 mole of dialkylaminoalkyl chloride, and 60 ml of dry dimethylformamide (DMF) was refluxed for 3 h after which the mixture was filtered to remove the inorganic precipitate, and the filtrate was vacuum evaporated on a water bath. The residue was dissolved in ether, and the ether solution was washed with water, dried with magnesium sulfate, and acidified with ether saturated with hydrochloride. The resulting precipitate was removed by filtration. Data on XIII and XIV are presented in Table 1.

5-β-Hydroxyethyl(tosyl)amino-2,3-tetramethylenethiophene (XV). A reaction mixture consisting of 20 g (0.061 mole) of XII, 4.25 g (0.066 mole) of ethylene chlorohydrin, and 150 ml of dry DMF was refluxed for 3 h, after which it was cooled, and the precipitate was removed by filtration. The filtrate was vacuum evaporated, and the resulting precipitate was recrystallized from methanol to give 14 g (65.3%) of a product with mp 121-122° (from methanol). Found: C 58.2; H 6.1%. $C_{17}H_{21}NO_3S_2$. Calculated: C 58.1; H 6.0%.

5-β-Carboxyethyl(tosyl)amino-2,3-tetramethylenethiophene (XVI). A 2.16-g (0.02 mole) sample of β-chloropropionic acid and 6.58 g (0.02 mole) of derivative XII were added to a solution of 0.8 g (0.02 mole) of sodium hydroxide in 20 ml of water, and the resulting solution was refluxed for 3 h. It was then poured into 200 ml of water, and the aqueous mixture was filtered to remove the turbidity. The filtrate was cooled and acidified with dilute hydrochloric acid, and the liberated oil was separated and dissolved in benzene. The benzene solution was purified with charcoal and diluted with petroleum ether, during which the liberated oil began to crystallize. Workup gave 2.3 g (35%) of a product with mp 129.5-130.5° (from 50% aqueous methanol). Found: C 57.0; H 5.7; S 16.9%. $C_{18}H_{21}NO_4S_2$. Calculated: C 57.0; H 5.6; S 16.9%.

5-β-Chloroethyl(tosyl)amino-2,3-tetramethylenethiophene (XVII). A 3.8-ml (0.019 mole) sample of thionyl chloride was added dropwise with stirring at room temperature to a solution of 3.8 g (0.011 mole) of XV in 12 ml of dry DMF, and the resulting solution was allowed to stand at room temperature for 2 h. It was then poured

over ice, and the aqueous mixture was extracted with ether. The ether extract was washed successively with water, sodium bicarbonate solution, and water and dried with magnesium sulfate. The ether was removed by distillation, and the residual oil was recrystallized from petroleum ether (bp 70°) to give 2.8 g (70%) of a product with mp 94-95°. Found: Cl 9.7; S 17.7%. $C_{17}H_{20}ClNO_2S_2$. Calculated: Cl 9.6; S 17.3%.

5-Tosylamino-4-thiocyanato-2,3-tetramethylenethiophene (XVIII). This compound, with mp 117-118° (from methanol), was obtained in 69% yield by the method described in [2]. Found: C 52.4; H 4.4; N 7.4; S 26.6%. $C_{16}H_{16}N_2O_2S_3$. Calculated: C 52.4; H 4.4; N 7.6; S 26.8%.

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ACETYLENIC α-AZIRIDINOCARBINOLS AND THE MECHANISM OF THEIR CONVERSION TO β-AZIRIDINOACROLEINS

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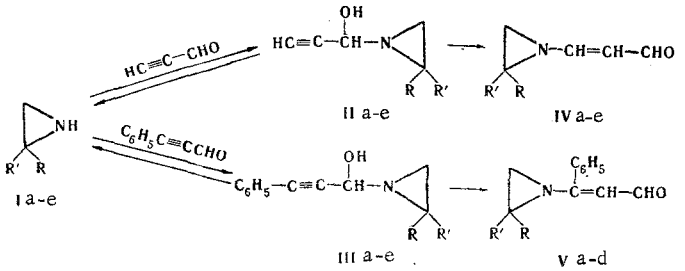
Acetylenic α-aziridinocarbinols were obtained by reaction of propiolaldehyde and phenylpropiolaldehyde with aziridine and its 2-substituted derivatives. The mechanism of the conversion of the latter to β-aziridinoacroleins was studied.

It is known [1-6] that aziridine and its 2-alkyl-substituted derivatives react with aliphatic and aromatic carbonyl compounds to give aziridinocarbinols, whereas only 3,4-addition products have been obtained up until now with α-unsaturated oxo compounds [5-7].

On the basis of PMR and IR spectroscopic studies we have established that α-aziridinocarbinols IIa-e and IIIa-e (Tables 1 and 2) are formed in 60-80% yields in the reaction of propiolaldehyde and phenylpropiolaldehyde with aziridines Ia-e at reduced temperature.



I-V a R = R′ = H; b R = H, R′ = CH_3; c R = R′ = CH_3; d R = H, R′ = C_2H_5; I-IV e R = H, R′ = $COOCH_3$

α-Aziridinocarbinols IIa-e and IIIa-e are colorless crystalline substances that at room temperature in both solutions and in the crystalline state undergo rearrangement to β-aziridinoacroleins IVa-e and Va-d, which exist in the form of cis-trans isomers in a ratio of 1:2.3 (Tables 3 and 4). The rate of isomerization

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