INVESTIGATION OF THE MOBILITY OF METHYLENE GROUP HYDROGEN ATOMS IN SOME DERIVATIVES OF 2-IMINOTHIAZOLIDIN-4-ONE

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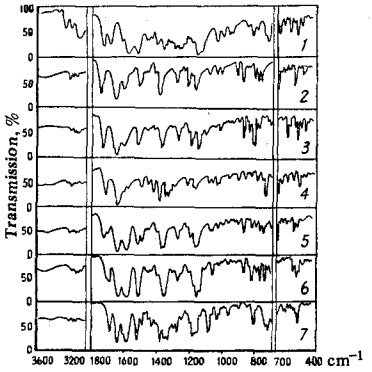
A study is made of the reaction of 2-arylamino- and 3-aryl-2-arylimino derivatives of thiazolidin-4-one with p-[N, N-di(2-chloroethyl)amino]benzaldehyde and p-nitroso-N, N-di(2-chloroethyl) aniline. It is shown that replacement of hydrogen at the endocyclic nitrogen atom of 2-iminothiazolidine-4-one raises mobility of hydrogen atoms in the methylene group in the order phenyl > p-tolyl > > benzyl. The results obtained are confirmed by IR spectroscopy.

From the literature it is known [1–3] that hydrogen atoms of the thiazolidin-4-one methylene group α to the carbonyl group possess a mobility which is shown



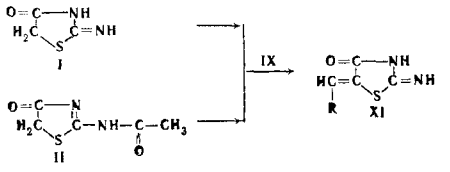
IR spectra of thiazolidin-4-one derivatives: 1) 5-[p-di(2'-chloroethyl)aminobenzylidene]-2-iminothiazolidin-4-one; 2) 3-phenyl-3-phenyliminothiazolidin-4-one; 3) 3-p-tolyl-2-tolyliminothiazolidin-4-one; 4) 3-benzyl-2-benzyliminothiazolidin-4-one; 5-7) 5-[p-di(2'-chloroethyl)aminobenzylidene) derivatives VI, VII, and VIII.

by the ability of thiazolindin-4-one derivatives to undergo condensation with aldehydes, ketones, and nitroso compounds, and diazo coupling to give benzylidene, azomethine and azo compounds.

The aim of the present work was to investigate the effect of substitution of hydrogen at the exo- and endocyclic nitrogen atoms in the 2-iminothiazolidin-4-one molecule on methylene group hydrogen mobility in the latter.

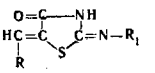
2-Iminothiazolidin-4-one (I), 2-acetaminothiazolin-4-one (II), 2-phenyl-, and 2-benzyl derivatives of 2-iminothiazolidin-4-one (III, IV, V), and also 3-phenyl-2-phenyliminothiazolidin-4-one (VI), 3-p-tolyl-2-p-tolylimino-, 3-benzyl 2-benzylimino derivatives of thiazolidin-4-one (VII, VIII) are synthesized, and reaction of the latter with p-[N, N-di(2-chloroethyl)amino] benzaldehyde (IX) and p-nitroso-N, N-di(2-chloroethyl)-aniline (X) is investigated.

Experiments showed that condensation of II with IX gives a benzylidene derivative, identical with the condensation product from I and IX, 5-[p-N, N-di(2'-chloroethyl)aminobenzylidene]thiazolidin-4-one (XI). (Chemical and IR spectroscopy results.)



The formation of benzylidene derivative XI by condensation of II and IX indicated that the above-mentioned reaction is accompanied by splitting off of the acetyl group from the 2-amino group of thiazolin-4-one, to give XI, which is a thiazolidin-4-one derivative. The results obtained are confirmed by the stability of II when heated in glacial acetic acid in the absence of aldehyde IX, as well as by results in the literature [4] regarding 5-benzylidene derivatives of thiazolindin-4-one existing in the imino form.

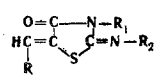
Condensation of 2-arylimino derivatives III and IV of thiazolidin-4-one with aldehyde IX in ethanol in the presence of a small amount of piperidine gave benzylidene derivatives XII, XIII in 10% and 2.0% yield respectively. 2-Benzylimino derivative V did not react with IX under the above reaction conditions.



XII R_1=C_6H_5
XIII R_1=p-CH_3—C_6H_4
R=$C_6H_4N(CH_2CH_2Cl)_2$-p

The nitro compound X, where the degree of polarization of the bond in the N=O group is less than that of the C=O group bond of aldehyde IX, did not react either with unsubstituted 2-iminothiazolidin-4-one, or with its 2-phenyl-, 2-p-tolyl- and 2-benzyl derivatives.

Hydrogen atoms of methylene groups of thiazolidin-4-one derivatives substituted at the endocyclic nitrogen atom are particularly mobile. Heating compounds VI, VII, and VIII with IX in ethanol in the presence of a small quantity of piperidine gave the 5-[p-N, N-di(2-chloroethyl)aminobenzylidene] derivatives XIV, XV, and XVI in 70, 44, and 26.6% yield respectively.



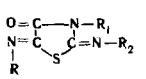
XIV R_1=R_2=C_6H_5
XV R_1=R_2=p-CH_3—C_6H_4
XVI R_1=R_2=—CH_2—C_6H_5
R=$C_6H_4N(CH_2CH_2Cl)_2$-p

The reactions of VI, VII, and VIII with nitroso compound X proceeded just as readily. 5-[p-N, N-Di(2'-

Benzylidene and Azomethine Derivatives of Thiazolid-4-one

Compound	Name	Mp, °C	Formula	Found, %				Calculated, %				Yield, %
				C	H	Cl	S	C	H	Cl	S	
XII	5-[p-Di(2'-chloroethyl)amino-benzylidene]-2-phenyliminothia-zolidin-4-one	195—196	$C_{20}H_{19}Cl_2N_3OS$	56.87	4.16	16.77	--	57.14	4.52	16.90	—	10.0
XIII	5-[p-Di(2'-chloroethyl)amino benzylidene]-2-p-tolyliminothia-zolidin-4-one	186—188	$C_{21}H_{21}Cl_2N_3OS$	57.74	4.41	16.06	—	58.06	4.83	16.35	—	2.0
XIV	5-[p-Di(2'-chloroethyl)amino-benzylidene]-3-phenyl-2-phenyl-iminothiazolidin-4-one	202	$C_{26}H_{23}Cl_2N_3OS$	62.82	4.58	14.02	—	62.9	4.64	14.31	—	70.0
XV	5-[p-Di(2'-chloroethyl)amino-benzylidene]-3-p-tolyl-2-p-tolyl-iminothiazolidin-4-one	197	$C_{28}H_{27}Cl_2N_3OS$	64.07	4.96	13.07	5.94	64.24	5.16	13.38	6.12	44.0
XVI	5-[p-Di(2'-chloroethyl)amino-benzylidene]-3-benzyl-2-benzyl-iminothiazolidin-4-one	150	$C_{28}H_{27}Cl_2N_3OS$	63.98	4.91	13.44	—	64.24	5.16	13.38	—	26.6
XVII	5-[p-Di(2'-chloroethyl)amino-phenylamino]-3-phenyl-2-phenyl-iminothiazolidin-4-one	180	$C_{25}H_{22}Cl_2N_4OS$	60.10	4.13	14.06	6.18	60.36	4.43	14.28	6.44	34.0
XVIII	5-[p-Di(2'-chloroethyl)amino-phenylimino]-3-p-tolyl-2-p-tolyl-iminothiazolidin-4-one	148	$C_{27}H_{26}Cl_2N_4OS$	—	—	13.6	5.93	—	—	13.33	6.09	34.3
XIX	5-p-Di-(2-chloroethyl)amino-phenylimino-3-benzyl-2-benzyl-iminothiazolidin-4-one	146	$C_{27}H_{26}Cl_2N_4OS$	—	—	13.25	6.18	—	—	13.33	6.09	15.4

chloroethyl) aminophenylimino] derivatives of VI, VII, and VIII, viz compounds XVII, XVIII, and XIX, were made by heating VI, VII, and VIII with X in methanol or ethanol containing a small amount of anhydrous potassium hydroxide. Compounds VI and X reacted together at 30°, VII and X at 55°, and finally X and the benzyl derivative VIII at 78°.



XVII $R_1=R_2=C_6H_5$
XVIII $R_1=R_2=p\text{-}CH_3\text{—}C_6H_4$
XIX $R_1=R_2=CH_2\text{—}C_6H_4$
$R=C_6H_4N(CH_2CH_2Cl)_2$

The experimental results show the high mobilities of the hydrogen atoms of the methylene group in compounds VI, VII, and VIII, evidently due to increased polarization of the π bond in the C=O group of the above-mentioned thiazolidin-4-one derivatives, arising on replacement of the hydrogen atoms at the endocyclic nitrogen by phenyl, p-tolyl, and benzyl groups. The yields of the benzylidene derivatives XIV, XV, and XVI, as well as the temperature conditions for the reactions between VI, VII, and VIII with nitroso compound X, make it possible to postulate that the degree of mobility of hydrogen atoms in the compounds is VI > VII > > VIII.

The effect of substitution at the endocyclic nitrogen atom on the polarization of the π bond in the carbonyl group of thiazolidin-4-one also follows from the IR absorption spectra of compounds VI, VII, VIII, and XIV, XV, XVI (see figure). Actually, the differences in electronegativity between substituents, leading to the sequence phenyl > p-tolyl > benzyl, leads to the same sequence for the variation in frequency of the valence vibrations of the C=O group. For compounds VI, VII, and VIII this frequency is, respectively, 1738, 1728, and 1712 cm^{-1}. The same frequency sequence was also found for 5-benzylidene derivatives, which had the following carbonyl valence vibration frequencies: 1700, 1721 cm^{-1} for XIV, 1705, 1693 cm^{-1} for XV, and 1692 cm^{-1} for XVI. From the spectra it can be seen that the bands at XIV and XV are doublets.

The lower frequencies of the C=O group valence vibrations found in the IR spectra of benzylidene derivatives compared with those for compounds VI–VIII, is probably due to π, π-conjugation of the C=O group. The spectra of compounds. VI, VII and XIV, XV, which have phenyl and p-tolyl substituents at the third ring nitrogen atom, show an intense absorption band in the 1380–1370 cm^{-1} region, to which we consider it possible to assign N—C valence vibration of the aromatic bond of the 3rd nitrogen atom. Its intensity is considerably less than with benzyl-substituted VIII and XVI. The exocyclic nitrogen atom C=N bond valence vibrations gave a very intense band, falling in the region 1650–1640 cm^{-1} in the spectra of VI–VIII, while in the spectra of XIV–XVI its value is about 10 cm^{-1} less. The valence vibrations of the C=C bond of benzylidene derivatives results in the appearance, in the region of vibrations of double bonds, of a rather intense band frequency 1575 cm^{-1} for XI, and of a band of frequency approximately 1587 cm^{-1} in the spectra of XIV, XV, and XVI. Aromatic absorption bands in the 1500–1600 cm^{-1} region do not interfere with separation of the vibration bands of the double bonds, considered above.

EXPERIMENTAL

A UR-10 (Zeiss, GDR) spectrophotometer was used to register the IR spectra of compounds VI, VII, VIII, XI, XIV, XV, and XVI, LiF, NaCl, and KBr prisms being used. The substances were tabletted with KBr for examination.

5-[p-N, N-Di(2'-chloroethyl)aminobenzylidene]-2-iminothiazolidin-4-one (XI). 0.23 g (0.002 mole I and 0.49 g (0.002 mole) IX were refluxed together for 30 min in 10 ml glacial AcOH containing 1 g fused NaOAc. The cold orange-red solution was mixed with 40 ml 20% NaCl solution, the precipitate filtered off, and washed on the filter with aqueous EtOH. Microcrystalline powder, bright yellow, mp 253° (ex AcOH), mass 0.35 g (50.8%). Found: C 48.51; H 4.48; Cl 20.30%, calculated: C 48.83; H 4.35; Cl 20.64%.

II and IX were condensed together under conditions similar to those described above for the reaction between I and XI. Mass 0.17 g (24.7%), mp 252.5° (ex AcOH). Found: Cl 20.51; S 8.96%, calculated: Cl 20.64; S 9.30%. The two compounds described above gave an undepressed mixed mp.

5-[p-N, N-Di(2'-chloroethyl)aminobenzylidene] derivatives (XII, XIII, XIV, XV, and XVI). Equimolecular quantities (0.005 mole) of III, IV, VII, VIII and aldehyde IX were refluxed together in EtOH (20–25 ml) for 2 1/2–4 hr. The EtOH was removed under vacuum at 25–30°. The viscous resinous products XII and XIII were recrystallized from AcOH, then recrystallized 3 times from EtOH—benzene. Compounds XIV and XV were recrystallized from EtOH—benzene, and XVI from acetone. They were bright yellow crystalline compounds.

5-[p-N, N-Di(2'-chloroethyl)aminophenylimino] derivatives (XVII, XVIII, XIX). 0.005 mole compounds VI, VII, VIII were dissolved, with heating, in 10–20 ml MeOH (VI and VII), then X (0.005 mole) and 0.001 mole anhydrous K_2CO_3 added in portions. Compound XV was obtained using a reaction temperature of 30°, XVI at 78°. The solutions of the reactants changed color as the reaction proceeded, from green to orange-red, and bright red crystals separated. After keeping in a refrigerator (10–12 hr) the precipitates were filtered off and washed with water. XVIII and XIX were recrystallized from MeOH, XVII from MeOH—benzene.

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