2,3-DIPHENYLTHIAZOLO[3,2-*a*]PYRIMIDINIUM SALTS

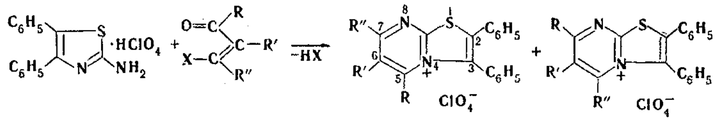
S. I. Shul'ga, N. F. Fursaeva,
and V. A. Chuiguk

UDC 547.789.6'859.3

The corresponding 2,3-diphenyl[3,2-*a*]pyrimidinium salts were obtained by the condensation of 4,5-diphenyl-2-aminothiazole perchlorate with β-diketones, β-chlorovinyl ketones, β-chlorovinyl aldehydes, and 1,1,3,3-tetraethoxypropane. The PMR spectra were used to prove the structures of the compounds obtained, particularly to select the structures of the isomeric salts obtained in the condensation with unsymmetrical β-diketones, β-chlorovinyl ketones, and β-chlorovinyl aldehydes. As a rule, the latter give one isomer – the γ-unsubstituted (relative to the bridge nitrogen atom) derivative.

We have previously [1-3] obtained the corresponding thiazolo[3,2-*a*]pyrimidinium salts by condensation of the salts of 2-aminothiazoles with β-diketones, β-chlorovinyl ketones, β-chlorovinyl aldehydes, and malonaldehyde bisdiacetal.

In the present communication we describe the reactions of the above carbonyl compounds with 2-amino-4,5-diphenylthiazole perchlorate (I). β-Diketones and β-chlorovinyl ketones react with I via the following scheme.



I II III

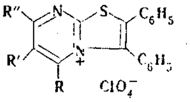
X = OH, Cl

The PMR spectra make it possible to establish both the general structures II and III and the structures of the isomeric products, which differ with respect to the position of the substituent in the pyrimidine ring.

First, the chemical shifts of the methyl groups in the 5 and 7 positions differ by ~0.5 ppm, and the 5-CH_3 signal lies at stronger field because of the shielding effect of 3-C_6H_5 [1-3, 6]. The selection of the structure in the case of the formation of isomeric II and III, which contain CH_3 in the 5 or 7 position, is therefore determined by the chemical shift of the methyl group. Thus the product of condensation with benzoylacetone (IIe) gives one signal of a methyl group at 2.56 ppm in its PMR spectrum, which corresponds to the 7-CH_3 group (for the product of condensation with acetylacetone, $\delta_{5\text{-}CH_3} = 1.98$ ppm and $\delta_{7\text{-}CH_3} = 2.52$ ppm). It follows from the PMR spectrum of the product of condensation with 1-ethoxyacetylacetone that this product is a mixture of isomers IIj ($R = CH_2OC_2H_5$, $R' = H$, $R'' = CH_3$) and IIIj ($R = CH_3$, $R' = H$, $R'' = CH_2OC_2H_5$) in a ratio of 1 : 1 (with respect to the intensities of $\delta_{5\text{-}CH_3} = 2.02$ ppm and $\delta_{7\text{-}CH_3} = 2.50$ ppm). Judging from the PMR spectrum, isomeric salts IIf and IIIf, for which $\delta_{CH_3} = 2.05$ and 2.55 ppm, are found in the crude product of the condensation of I with methyl β-chlorovinyl ketone in a ratio of 3.2, while the spin–spin coupling constants of the pyrimidinium protons are 5 and 7 Hz, respectively. The first isomer was isolated in pure form by fractional recrystallization.

Kiev Technologic Institute of the Food Industry. T. G. Shevchenko Kiev State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 629-631, May, 1972. Original article submitted January 21, 1971.

TABLE 1. 2,3-Diphenylthiazolo[3,2-*a*]pyrimidinium Salts (II)



Compound	R	R′	R″	Mp, °C	Crystallization solvent	Empirical formula	Found, %		Calc., %		Yield, %
							S	N	S	N	
IIa	CH_3	H	CH_3	240—243	Ethanol	$C_{20}H_{17}ClN_2O_4S$	7,75	—	7,69	—	86
IIb	CH_3	CH_3	CH_3	188—189	Methanol	$C_{21}H_{19}ClN_2O_4S$	7,25	6,49 6,54	7,44	6,50	67
IIc	CH_3	C_2H_5	CH_3	230	Butanol	$C_{22}H_{21}ClN_2O_4S$	6,98	6,63 6,60	7,20	6,30	69
IId	C_6H_5	H	C_6H_5	262—263	Ethanol	$C_{30}H_{21}ClN_2O_4S$	6,06	5,70	5,93	5,17	52
IIe	C_6H_5	H	CH_3	198—200	Butanol	$C_{25}H_{19}ClN_2O_4S$	6,73	—	6,69	—	75
IIf	CH_3	H	H	250—251	Ethanol	$C_{19}H_{15}ClN_2O_4S$	8,19	7,10	7,95	7,10	34*
IIg	H	H	H	220—222	Methanol	$C_{18}H_{13}ClN_2O_4S$	8,40	7,47	8,24	7,20	79
IIh	CH_3	CH_3	H	170—171	Methanol	$C_{20}H_{17}ClN_2O_4S$	7,80	7,01	7,69	6,72	75
IIi	—$(CH_2)_4$—		H	192—194	n-Propyl alcohol	$C_{22}H_{19}ClN_2O_4S$	7,39	6,31	7,24	6,32	56

---

* The yield of the mixture of isomers.

A second factor in the PMR spectra that makes it possible to establish the structures of the compounds obtained is the character of the signal of the phenyl group of the pyrimidine ring [4]. A phenyl group in the 5 position is displayed in the spectrum as a singlet, while the same group in the 7 position gives two groups of signals with an intensity ratio of 2 : 3, which is explained by the influence of the neighboring nitrogen atom. The signal of the pyrimidine phenyl group in IIe is not split, which confirms that it is in the 5 position.

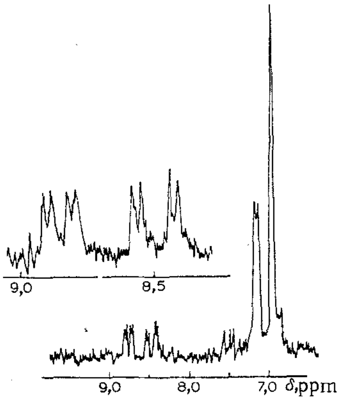


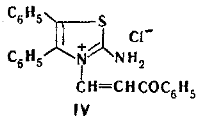
Fig. 1. PRM spectrum of IIg.

A third factor in the PMR spectra that we used to establish the structures of the reaction products involves the spin–spin coupling constants between the 5- and 6-, and 7- and 6-hydrogen atoms of the pyrimidine ring [5]. Just as in other similar salts, $J_{H_5H_6} = 7$ Hz, and $J_{H_7H_6} = 5$ Hz. When there is no phenyl group in the 3 position, $\delta_{H_5} > \delta_{H_7}$, while in our case, on the other hand, $\delta_{H_7} > \delta_{H_5}$, which is also explained by shielding of the proton in the 5 position by the phenyl group.

1,1,3,3-Tetraethoxypropane reacts with I to form IIg. The PMR spectrum of IIg is shown in Fig. 1. The protons in the 5 and 7 positions of the pyrimidine ring give the theoretical ABX pattern (the AB portion) and $J_{H_5H_6} = 7$ Hz, while $J_{H_7H_6} = 5$ Hz and $\delta_{H_7} > \delta_{H_5}$.

β-Chlorovinyl aldehydes react with I in one direction to give II, which are unsubstituted in the γ-position relative to the bridge nitrogen atom. The structures of these salts are also confirmed by the PMR spectra. In particular, as a consequence of the shielding effect of the 3-phenyl group, 5-CH_3 has a chemical shift of 2.03 ppm, while $\delta_{5\text{-}CH_3} = 2.25$ ppm instead of the "normal" values 2.9-3.0 and 3.0-3.1 ppm, respectively. The thiazolopyrimidinium salts obtained are presented in Table 1.

Quaternary salts II with a methyl or methylene group in the 5 or 7 positions give polymethine dyes.



IV

The reaction of phenyl β-chlorovinyl ketone with 2-amino-4,5-diphenylthiazole (the base) gives product IV, the structure of which was assumed on the basis of an analogy with the products obtained in [6] and also on the basis of the IR spectrum, in which a double-peaked band is observed at 3300-3500 cm^{-1}, the region characteristic for the amino group, together with a peak at 1690 cm^{-1}, which we ascribe to the frequency of a carbonyl group (ν_{CO}) conjugated with a positively charged nitrogen atom.

EXPERIMENTAL

The IR spectra of KBr pellets were determined with a UR-20 spectrometer. The PMR spectra of trifluoroacetic acid solutions were recorded with a Varian A-60A spectrometer. The chemical shifts were determined on the δ scale with respect to hexamethyldisiloxane (HMDS).

Condensation of I with β-Diketones. A mixture of 4 mmole of I and 4-8 mmole of the appropriate β-diketone was heated at 120-140° for 30 min to 2 h or refluxed in alcohol for 1-2 h. The product was then washed with methanol and ether and recrystallized. When the condensation was carried out in alcohol, the crystals that precipitated after cooling were separated; an additional amount of product was isolated from the filtrate by precipitation with ether. The reaction of I with 1-ethoxyacetylacetone was carried out similarly with 1 g (4 mmole) of I, 9.6 ml (4.2 mmole) of 1-ethoxyacetylacetone, and 3 ml of methanol to give 0.9 g (69%) of product. The product was a mixture of isomers IIj and IIIj in a ratio of 1 : 1 and had mp 110-111° (from methanol). Found: S 7.07%. $C_{22}H_{21}ClN_2O_5S$. Calculated: S 7.20%.

Condensation of I with β-Chlorovinyl Aldehydes. A mixture of 4 mmole of I, 6 mmole of the appropriate β-chlorovinyl aldehyde, and 3 ml of methanol was heated on a water bath for 10-20 min. The mixture was cooled, and the precipitated reaction product was separated and washed with ether and recrystallized. Product IIf was obtained by the method in [5].

2,3-Diphenylthiazolo[3,2-*a*]pyrimidinium Perchlorate (IIg). A mixture of 1 g (3 mmole) of I, 1.1 ml (5 mmole) of 1,1,3,3-tetraethoxypropane, and 3 ml of ethanol was heated on a water bath. The reaction product precipitated after 5 min. The reaction mixture was cooled, and the product was separated, washed with ether, and recrystallized.

2-Amino-4,5-diphenyl-3-(3-phenyl-1-propen-3-on-1-yl)thiazolium Chloride (IV). A mixture of an alcohol solution of 1.77 g (7 mmole) of 2-amino-4,5-diphenylthiazole and 3 ml (1.8 mmole) of phenyl β-chlorovinyl ketone was refluxed for 1 h and cooled, and the precipitate was separated and washed with ether to give 1.17 g (49%) of a product with mp 156-157° (from ethyl acetate–methanol). Found: S 7.99%. $C_{24}H_{19}ClN_2OS$. Calculated: S 7.65%.

LITERATURE CITED

1. S. I. Shul'ga and V. A. Chuiguk, Ukr. Khim. Zh., 36, 483 (1970).
2. S. I. Shul'ga and V. A. Chuiguk, Ukr. Khim. Zh., 37, 257 (1971).
3. S. I. Shul'ga and V. A. Chuiguk, Ukr. Khim. Zh., 37, 350 (1971).
4. A. Le Berre and C. Renault Bull. Soc. Chim. France, 3139 (1969).
5. L. W. Werbel, A. Curry, E. F. Elslager, C. A. Hess, M. P. Hutt, and C. Gongstron, J. Heterocycl. Chem., 6, 787 (1969).
6. S. I. Shul'ga and V. A. Chuiguk, Khim. Geterotsikl. Soedin., 632 (1972).
7. A. N. Nesmeyanov and M. I. Rybinskaya, Dokl. Akad. Nauk SSSR, 118, 297 (1958).