1-Diazo-3-(8-quinolylmercapto)propanones (VIa-c) (General Method). These compounds were similarly obtained from 0.02 mole of the potassium salt of 8-mercaptoquinoline and 0.02 mole of diazo ketone IIa-c (see Table 1).

LITERATURE CITED

1. V. G. Kartsev, T. S. Pokidova, A. V. Dovgilevich, and A. S. Nabatov, Khim. Geterotsikl. Soedin., No. 4, 514 (1984).
2. A. L. Fridman, G. S. Ismagilova, V. S. Zalesov, and S. S. Novikov, Usp. Khim., 41, 722 (1972).
3. V. G. Kartsev and T. S. Pokidova, Khim. Geterotsikl. Soedin., No. 3, 415 (1982).
4. F. Arndt and B. Eistert, Chem. Ber., 68, 200 (1935).

DIAZO CARBONYL DERIVATIVES OF HETEROCYCLES.

5.* INTRAMOLECULAR CYCLIZATION OF 2-HETARYLMERCAPTOALKYL-DIAZO KETONES. SYNTHESIS OF CONDENSED 1,3-THIAZIN-5-ONES

V. G. Kartsev, T. S. Pokidova,
and A. V. Dovgilevich

UDC 547.235.41'284'869.1'785.5'789.6'
787.3'836.7'831.1.07:542.97:543.
422

The intramolecular heterocyclization of 2-benzazolylmercaptoalkyl diazomethyl ketones under the influence of acidic agents leads to 1,3-thiazino[2,3-b]benzimidazole, 1,3-thiazino[2,3-b]benzothiazolium, and 1,3-thiazino[2,3-b]benzoxazolium systems. Under similar conditions 2-quinolylmercaptoalkyl diazomethyl ketones form 1,3-thiazino[2,3-a]quinolinium systems.

We have previously reported a new method for obtaining a thiazine ring by intramolecular alkylation of the sulfur atom in the corresponding thioureidoalkyl α-diazo ketones under the influence of acidic agents [2]. However, the described method does not make it possible to obtain condensed heterocyclic systems that contain a 1,3-thiazine ring. In addition, the synthesis of the starting diazo ketones is extremely laborious. Nevertheless, precisely condensed 1,3-thiazines are included in the structures of valuable biologically active compounds such as antibiotics [3]. We have recently shown that acid-catalyzed heterocyclization at the nitrogen atom of the imidazole ring in 2-benzimidazolylmercaptomethyl diazomethyl ketone leads to 5-keto-3,4,5,6-tetrahydro-1,3-thiazino[2,3-b]benzimidazole [4].

In order to expand the possibilities of the use of intramolecular alkylation of diazo carbonyl derivatives of 2-mercaptoheterocycles for the synthesis of various condensed 1,3-thiazines, in the present research we studied the transformations of 2-hetarylmercaptoalkyl diazomethyl ketones Ia-c, VIIIa-d, and XIa-c, which we obtained in [1], under the influence of acidic agents.

We found that the introduction of a methyl group into the side chain (Ib) promotes heterocyclization and that the corresponding 1,3-thiazino[2,3-b]benzimidazole VIb is formed more easily. Thus the formation of VIb is observed at room temperature even without the participation of an acid. The mechanism of this transformation evidently includes self-catalysis by the acidic proton of the imidazole ring (via an intramolecular process, as shown in scheme A, or via intermolecular pathway B); the nucleophilicity of the nitrogen atom of the imidazole ring increases in intermediates IIb and IIIb, and this also promotes heterocyclization. Let us note that the thermal transformation of diazo ketone Ia also leads to cyclic compound VIa.

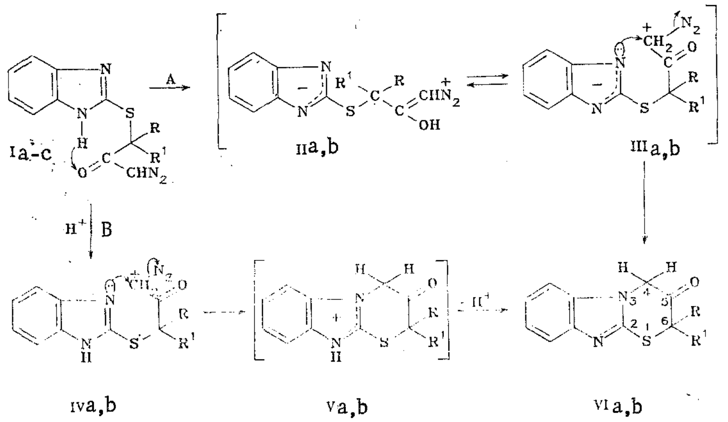
The acid-catalyzed heterocyclization of diazo ketone Ib, which leads to VIb (pathway B), also proceeds more rapidly as compared with homolog Ia. The acceleration of the reaction is

---

*See [1] for communication 4.

Branch of the Institute of Chemical Physics, Academy of Sciences of the USSR, Chernogolovka 142432. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 635-639, May, 1984. Original article submitted September 17, 1983.

0009-3122/84/2005-0508$08.50

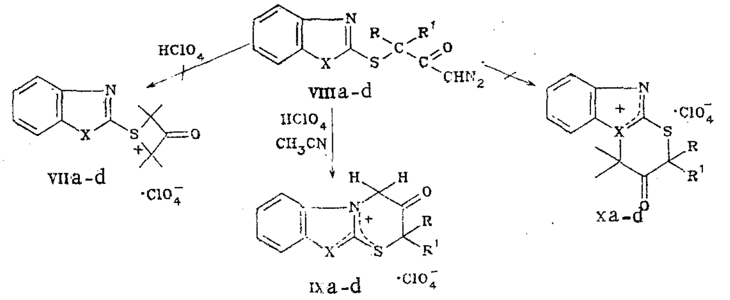


a $R=R^1=H$; b $R=H$, $R^1=CH_3$; c $R=R^1=CH_3$

apparently associated with a decrease in the negative entropy of activation, since the number of degrees of freedom of the motion of the side chain of starting diazo ketone I decreases with the introduction of a substituent, and the probability of a cyclic process increases.

Moreover, attempts to realize the similar transformation of sterically hindered diazo ketone Ic under the influence of various acidic agents (acetic, sulfuric, and perchloric acids and boron trifluoride etherate) did not lead to the desired result. This may be associated with steric hindrance of the two methyl groups both in the intramolecular alkylation step and in the protonation step; in this case the preferred pathway may not be protonation of the more remote [from the bulky $C(CH_3)_2$ group] nitrogen atom of the imidazole ring, which decreases the nucleophilicity sharply and, consequently, hinders heterocyclization.

The reaction terminates with the formation of onium compounds IXa-d in the action of 60% perchloric acid in acetonitrile on diazo ketones VIIIa-d, which contain benzoxazole and benzothiazole fragments. Neither intramolecular S-alkylation to give thietanes VIIa-d nor cyclization at the oxygen or sulfur atoms of the azole ring (Xa-d) occurs in this case because of the weak nucleophilicity of the corresponding atoms, since their electron pairs are included in an aromatic sextet:



VII—X a-d a $X=O$, $R=R^1=H$; b $X=O$, $R=H$, $R^1=CH_3$; c $X=S$, $R=R^1=H$; d $X=S$, $R=H$, $R^1=CH_3$

The conditions under which the reaction is carried out (slow addition of perchloric acid to a solution of the diazo ketone in CH_3CN at room temperature) make it possible to avoid a side process — Ritter reaction with the participation of acetonitrile and the formation of an oxazole ring in the side chain [5]. The stability of cyclic ammonium salts IXa-d is apparently due to the possibility of delocalization of the positive charge over three heteroatoms (N, O, and S in IXa,b or N, S, and S in IXc,d) due to participation of the d electrons of sulfur and the p electrons of oxygen in conjugation.

The 5-oxo-5,6-dihydro-4H-1,3-thiazino[2,3-b]benzoxazolium (IXa,b) and 5-oxo-5,6-dihydro-4H-1,3-thiazino[2,3-b]benzothiazolium (IXc,d) salts obtained in this way are crystalline substances that decompose explosively when they are heated above their melting points. The introduction of a substituent into the side chain has virtually no effect on the yields of IX.

Under similar conditions 1-diazo-3-(2-quinolylmercapto)propanones XIa-c undergo cyclization to 5-oxo-5,6-dihydro-4H-1,3-thiazino[2,3-a]quinolinium perchlorates XIIa-c:

TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
VIa	183*	58,7	3,9	13,6	$C_{10}H_8N_2OS$	58,8	3,9	13,7	90
VIb	78	60,5	4,5	12,6	$C_{11}H_{10}N_2OS$	60,6	4,6	12,8	92
IXa	190	39,4	2,4	4,5	$C_{10}H_8NO_2S^+ \cdot ClO_4^-$	39,3	2,6	4,6	85
IXb	225	41,4	3,0	4,3	$C_{11}H_{10}NO_2S^+ \cdot ClO_4^-$	41,3	3,1	4,4	92
IXc	216	37,3	2,4	4,3	$C_{10}H_8NOS_2^+ \cdot ClO_4^-$	37,3	2,5	4,4	92
IXd	229	39,2	2,8	4,1	$C_{11}H_{10}NOS_2^+ \cdot ClO_4^-$	39,3	3,0	4,2	95
XIIa	210	45,3	3,0	4,2	$C_{12}H_{10}NOS_2^+ \cdot ClO_4^-$	45,6	3,2	4,4	98
XIIb	196	47,1	3,5	4,2	$C_{13}H_{12}NOS^+ \cdot ClO_4^-$	47,3	3,6	4,3	98
XIIc	160	48,7	4,2	3,9	$C_{14}H_{14}NOS^+ \cdot ClO_4^-$	48,9	4,1	4,1	95

*With decomposition.

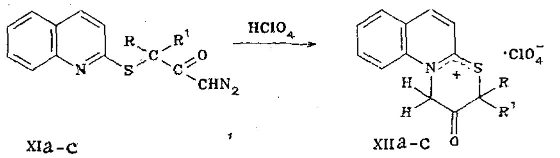
TABLE 2. Spectral Characteristics of the Compounds Obtained

Compound	PMR spectrum, δ, ppm (J, Hz)	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}
VIa*	7,0—7,7 (4H, m., Ar); 4,7 (2H, s, 4-H); 3,65 (2H, s, 6-H)	212 (4,2), 252 (3,9), 274 (4,01), 280 (4,01)	1720 (C=O), 1580 (C=C)
VIb*	7,14—7,7 (4H, m, Ar); 4,83—5,21 (2H, dd, J=18, 4-H); 1,5 (3H, d, J=7, $CHCH_3$); 4,37 (1H, q, J=7, $CHCH_3$)	216 (4,32), 253 (3,8), 272 (3,89)	1725 (C=O), 1580 (C=C)
IXa†	7,62—7,83 (4H, m., Ar); 5,24 (2H, s, 4-H); 4,27 (2H, s, 6-H)	230 (3,70), 282 (3,89), 288 (3,87)	1700 (C=O), 1580 (C=C), 1245 (ClO_4^-)
IXb	7,74—7,88 (4H, m, Ar); 5,12 and 5,59 (2H, dd, J=18, 4-H); 1,77 (3H, d, $CHCH_3$); 4,84 (q, J=7, $CHCH_3$)	232 (3,72), 282 (3,75), 289 (3,73)	1695 (C=O), 1580 (C=C), 1245 (ClO_4^-)
IXc	7,75—8,2 (4H, m, Ar); 5,4 (2H, s, 4-H); 4,24 (2H, s, 6-H)	233 (3,4), 261 (3,79), 318 (4,19)	1730 (C=O), 1580 (C=C), 1250 (ClO_4^-)
IXd	7,75—8,19 (4H, m, Ar); 5,17 and 5,76 (2H, dd, J=18, 4-H); 1,76 (3H, d, J=7, $CHCH_3$); 4,69 (1H, q, $CHCH_3$)	232 (3,28), 260 (3,26), 318 (3,75)	1725 (C=O), 1580 (C=C), 1240 (ClO_4^-)
XIIa†	7,95—8,83 (6H, m, Ar); 5,75 (2H, s, 4-H); 4,23 (2H, s, 6-H)	242 (3,82), 265 (4,01), 272 (4,01), 332 (4,1)	1720 (C=O), 1580 (C=C), 1250 (ClO_4^-)
XIIb	7,9—8,78 (6H, m, Ar); 5,37 and 6,12 (2H, dd, J=18, 4-H); 1,7 (3H, d, J=7, $CHCH_3$); 4,67 (1H, q, J=7, $CHCH_3$)	242 (3,80), 265 (4,47), 271 (4,47), 352 (4,5), 367 (4,47)	1720 (C=O), 1580 (C=C), 1250 (ClO_4^-)
XIIc	7,89—8,82 (6H, m, Ar); 5,81 (2H, s, 4-H); 1,81 (6H, s, 2-CH_3)	240 (4,12), 262 (4,12), 268 (4,09), 352 (4,20), 362 (4,17)	1730 (C=O), 1580 (C=C), 1245 (ClO_4^-)

---

*The UV spectra were recorded in methanol.

†The UV spectra were recorded in water—acetonitrile (9:1).



XIa-c

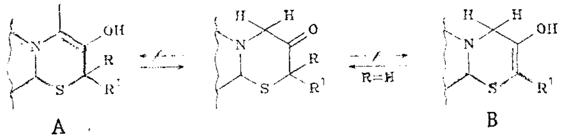
XIIa-c

XI, XII a R=R¹=H; b R=H, R¹=CH_3; c R=R¹=CH_3

In addition to two heteroatoms (N and S), the aromatic system of quinoline also participates in delocalization of the positive charge and stabilization of salts XII. As in the examples described above, which lead to onium compounds, an effect of the substituents on the yields of salts XIIa-c was not noted.

It is apparent from Table 2 that characteristic absorption bands of the carbonyl group in 1,3-thiazin-5-ones at 1695-1730 cm^{-1} and of C=C and C=N groups at 1570-1580 cm^{-1} [2] are observed in the IR spectra of these compounds; absorption bands of the diazo group of the starting diazo ketones at 2100 cm^{-1} and, for VIa,b, bands of NH vibrations are absent in the spectra. At the same time, absorption at 1245 cm^{-1}, which is characteristic for organic perchlorates [6], is observed in the spectra of IXa-d and XIIa-c. In the PMR spectra of VIa, IXa,c, and XIIa, in which methyl substituents in the thiazine ring (VIa, IXa, and XIIa) are absent or two methyl substituents (IXc) are present, signals of protons of a methylene group in the 4 position are observed in the form of singlets that are shifted to weak field as compared with the signals of the 6-H protons; the transition from covalent VIa to onium salts IXa,c and XIIa leads to a significant shift of the signals of the protons of both methylene groups to weak field. This assignment of the signals was made on the basis of a comparison of the spectra of these compounds with the spectra of their 6,6-dimethyl-substituted derivatives, in which the 6-H protons are observed in the form of quartets. The introduction of a methyl substituent in the 6 position (VIb, IXb,d, and XIIb) leads to nonequivalence of the protons attached to $C_{(4)}$; two doublets with geminal coupling constant J = 18 Hz, which is characteristic for 6-monosubstituted 1,3-thiazines [2], appear in the spectra in this case (see Table 2).

It should be noted that the presence of even traces of enol forms of the A and B types was not detected either in the case of thiazinobenzazoles VI and IX or in the case of thiazinoquinolines XII:



Thus the intramolecular heterocyclization of 2-hetarylmercaptoalkyl diazomethyl ketones is a convenient method for the synthesis of compounds that contain a thiazine ring condensed with a heterocyclic system.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a Specord IR-75 spectrometer. The UV spectra of solutions in water—acetonitrile (9:1) were obtained with a Specord UV-vis spectrophotometer. The PMR spectra of solutions in trifluoroacetic acid and d_6-acetone were recorded with a Tesla BS-497 spectrometer. The purity of the substances was monitored by thin layer chromatography (TLC) in benzene—acetonitrile and benzene—ethyl acetate systems on Silufol UV-254 plates.

The physicochemical properties of the compounds obtained are presented in Tables 1 and 2.

1-Diazo-3-(2-benzazolylmercapto)propanones Ia-c and VIIIa-d and 1-diazo-3-(2-benzoquinolylmercapto)propanones XIa-c were synthesized by the methods described in [1].

5-Oxo-3,4,5,6-tetrahydro-1,3-thiazino[2,3-b]benzimidazoles (VIa,b) (General Method). A 5-ml sample of acetic acid was added to 0.02 mole of diazo ketone Ia-c. After nitrogen evolution had stopped completely (after 4 h), the acid was removed by distillation, 3 ml of water was added to the residue, and the mixture was made alkaline to pH 7-8 and extracted with methylene chloride (five 2-ml portions). The extract was evaporated *in vacuo*, and the residue was separated with a column packed with silica gel by elution with benzene—ethyl acetate (1:1). Fractions with R_f 0.37 for VIa and R_f 0.42 for VIb were isolated.

5-Oxo-5,6-dihydro-4H-1,3-thiazino[2,3-b]benzoxazolium and 5-Oxo-5,6-dihydro-4H-1,3-thiazino[2,3-b]benzothiazolium Perchlorates (IXa-d) (General Method). A 0.5-ml sample of 60% perchloric acid was added with stirring to a solution of 0.025 mole of diazo carbonyl compound Va-d in 3 ml of acetonitrile. After nitrogen evolution had stopped completely, excess ether was added, and the resulting precipitate was recrystallized from acetonitrile—ether (10:1) to give IXa-d (see Tables 1 and 2 for the properties of these compounds).

5-Oxo-5,6-dihydro-4H-1,3-thiazino[2,3-a]quinolinium perchlorates XIIa-c were similarly obtained.

LITERATURE CITED

1. V. G. Kartsev, T. S. Pokidova, and A. I. Dovgilevich, Khim. Geterotsikl. Soedin., No. 5, 632 (1984).
2. V. G. Kartsev, A. M. Sipyagin, N. F. Sepetov, and L. A. Sibel'dina, Khim. Geterotsikl. Soedin., No. 10, 1327 (1980).
3. A. Beil, A. Candliff, P. Reynolds, M. Richmond, and M. Warring, in: Molecular Foundations of the Action of Antibiotics [Russian translation], Mir, Moscow (1975), p. 114.

4. V. G. Kartsev and T. S. Pokidova, Khim. Geterotsikl. Soedin., No. 3, 415 (1982).
5. R. M. Acheson and M. W. Cooper, J. Chem. Soc., Perkin Trans. I, No. 5, 1185 (1980).
6. W. T. Flowers, A. M. Freitas, and G. Holt, J. Chem. Soc., Perkin Trans I, No. 4, 1119 (1981).

TRIFLUOROACETYLATION OF 9-METHYLCARBAZOLE. EXAMPLE OF THE FORMATION OF A TRIARYLFLUOROETHANE IN THE HETEROCYCLIC SERIES

E. E. Sirotkina, N. V. Moskalev,
and I. G. Shabotkin

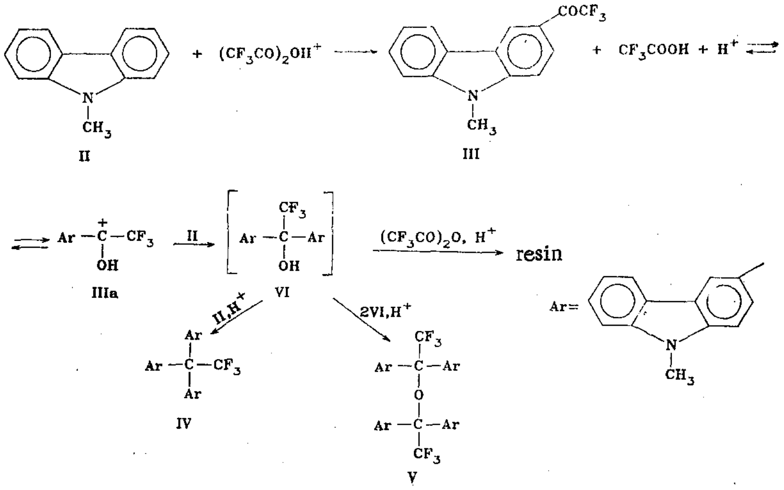
UDC 547.759.32:547.412.62

It is shown that the trifluoroacetylation of 9-methylcarbazole proceeds regiospecifically in the 3 position of the ring. 1,1,1-Tris(9-methyl-3-carbazolyl)-2,2,2-trifluoroethane and 1,1,1',1'-tetrakis(9-methyl-3-carbazolyl)-2,2,2,2',2',-2'-hexafluorodiethyl ether were also isolated from the reaction mixture. Bis(trifluoroacetyl) derivatives were not detected. Only a 3-trifluoroacetyl derivative is formed when the reaction is carried out by heating in the presence of pyridine.

It is known that carbazole (I) is trifluoroacetylated at the heteroatom [1]. 9-Methyl-1-trifluoroacetylcarbazole was obtained through the corresponding 1,2,3,4-tetrahydracarbazole derivative [2].

We have observed that 9-methylcarbazole (II) reacts with trifluoroacetic anhydride (TFAn) in the absence of a catalyst at room temperature to give 9-methyl-3-trifluoroacetylcarbazole (III) and a small amount of resinous products. Resin formation becomes predominant when the temperature is raised to 100-120°C. The addition of condensing agents such as boron trifluoride etherate, aluminum chloride, and tin tetrachloride leads to complete resinification of the reaction mass. The reaction does not take place in the presence of equimolar (with respect to product II) amounts of pyridine at room temperature, and only ketone III is formed when the mixture is heated to 100-120°C. We noted that a significant induction period, which was absent when a mixture of TFAn and trifluoroacetic acid (TFAc) was used, was observed in the course of the reaction when TFAn that had been thoroughly purified by repeated distillation over phosphorus pentoxide was used. This indicates that the process evidently takes place under conditions of self-catalysis by the liberated TFAc.

$$(CF_3CO)_2O + CF_3COOH \rightleftarrows (CF_3CO)_2OH^+ + CF_3COO^-$$



S. M. Kirov Tomsk Polytechnic Institute, Tomsk 634004. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 640-642, May, 1984. Original article submitted July 19, 1983; revision submitted October 12, 1983.