

4-AZAINDANE-1,3-DIONE DERIVATIVES.

III.* REACTIVITIES AND PROTOTROPIC TRANSFORMATIONS OF NEW 4-AZAINDANE-1,3-DIONES

A. Ya. Ozola, É. I. Stankevich,
S. V. Kalnin',† and O. Ya. Neiland

UDC 547.834.2'835:542.938.942.944;
543.422.4

New 4-azaindane-1,3-dione derivatives were synthesized from 3-ethoxalyl-5-R-cyclopentane-1,2,4-trione and aliphatic β -aminovinylcarbonyl compounds. The halogenation, reduction, and hydrolysis of the synthesized compounds were investigated. The prototropic equilibria of 4-azaindane-1,3-diones were studied.

Continuing our investigation of 4-azaindane-1,3-dione derivatives, which are generating increasing interest in connection with the detection of photosensitivity in some of them [2, 3], we have made a more detailed study of our previously proposed method [1, 4] for the synthesis of these compounds. The main product of the condensation of 3-ethoxalyl-5-R-cyclopentane-1,2,4-triones (Ia,d) and aliphatic β -aminovinylcarbonyl compounds (IIa-c) are 2-R-5-methyl-6-R'-7-ethoxycarbonyl-4-azaindane-1,3-diones (IIIa-d). In two cases, in addition to the chief condensation products IIIa,b, we were able to isolate enamines IVa,b, the structure of which was proved by synthesis from IIIa and IVa of identical bromo derivatives VIIa [5]. The elevated frequencies of the keto groups (ν_{CO} 1742 and 1772 cm^{-1}) constitute evidence for the diketo structure of VIIa. We suppose that the products of the decomposition of the starting β -aminovinylcarbonyl compounds (IIa,b) are the source of the nitrogen of the amino group of IVa,b. 5-Methyl-3-ethoxalylcyclopentane-1,2,4-trione (Ia) is probably iminated prior to cyclization, inasmuch as we were unable to obtain imines IVa,b from diketone IIIa,b by direct reaction with ammonium acetate. The position of the amino group in IVa,b therefore depends on the activity of the keto groups of a starting trione Ia. Inasmuch as the $\text{C}_1=\text{O}$ and $\text{C}_2=\text{O}$ groups most readily undergo nucleophilic attack, 3-amino-2,5-dimethyl-6,7-di(ethoxycarbonyl)-4-azainden-1-one (IVa) should be formed as a result of cyclization. The bright-red color of IVa also constitutes evidence for its enamine structure [5]. Hydrolytic splitting out of an amino group does not occur in acidic media, and only the hydrochloride (VIIa) of enamine IVa is formed.

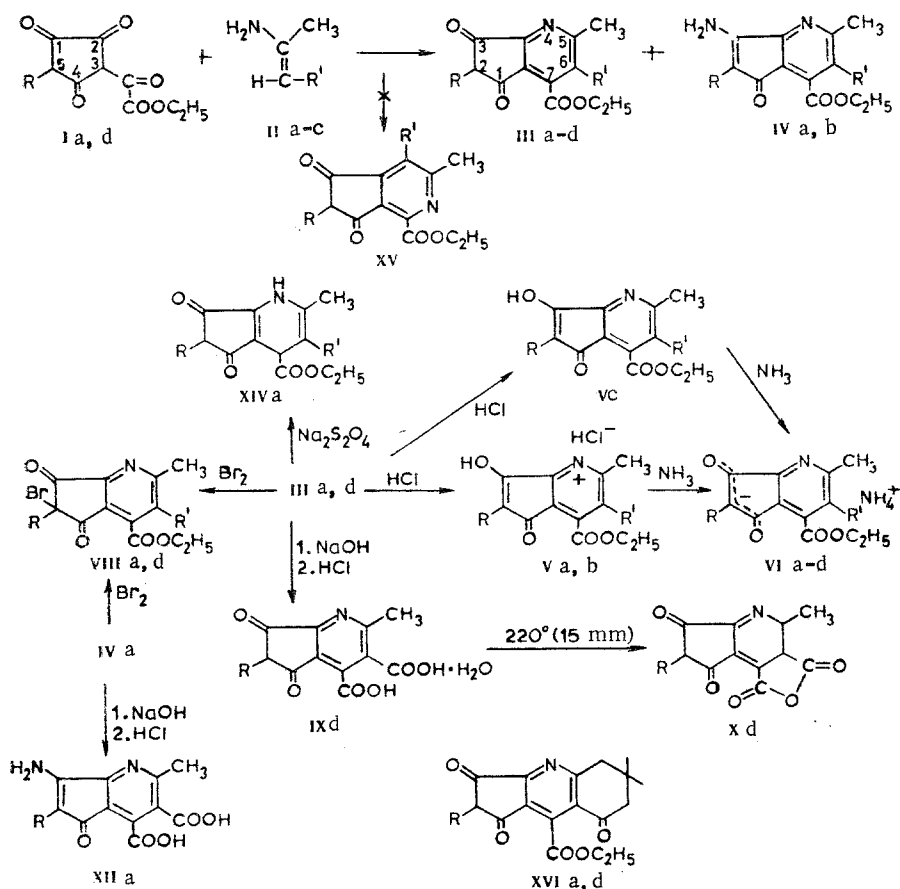
The formation of isomers III and XV is theoretically possible in the condensation of I and II. However, we have proved that the compounds obtained in this research are 4-azaindane-1,3-dione derivatives (IIIa-d). First, dicarboxylic acids IXd and XIIa, which are converted by heating *in vacuo* to anhydrides as evidenced by the appearance in the IR spectra of bands at 1841-1859 and 1796 cm^{-1} , were obtained as a result of alkaline hydrolysis of IIIId and IVa. This confirms the presence of nitrogen in the 4 positions of IIIId and IVa, inasmuch as XV is incapable of forming an anhydride. Second, IIIa was reduced with sodium hydrosulfite to dihydropyridine XIVA, which is similar to the previously obtained 2,5-dimethyl-6-ethoxycarbonyl-7-phenyl-4,7-dihydro-4-azaindane-1,3-dione [6]. Compounds IIIa-d contain crystallization water, which is not lost even on prolonged heating *in vacuo*. The IR spectra contain absorption bands at 3000-3500 cm^{-1} , which correspond to ν_{OH} . In strongly acidic media IIIa,b form yellow, easily hydrolyzed hydrochlorides Va,b. The action of ammonia on hydrochlorides Va,b gave bright-red ammonium salts VIa,b, the IR spectra of which

*See [1] for communication II.

†Deceased.

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga. Riga Polytechnic Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 256-262, February, 1976. Original article submitted February 19, 1975.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50.



I, IX, X, XII, XVI a R=CH₃; d R=C₆H₅; II a R'=COOC₂H₅; b R'=COOC₅H₁₁; c R'=CN; III-VIII, XIV, XV a R=CH₃, R'=COOC₂H₅; b R=CH₃, R'=COOC₅H₁₁; c R=CH₃, R'=CN; d R=C₆H₅, R'=COOC₂H₅.

contain intense bands at 1530-1536 cm⁻¹, which are characteristic for equalized π -electron density of an anionic system [7]. Particularly pronounced equalization of the π -electron density is manifested in the case of VI d, which has a band at 1515 cm⁻¹. The observed sharp changes in the colors of III a-d depend on the pH of the media and are associated with the existence of these compounds in various tautomeric forms. The literature data [8, 9] and our studies of the tautomeric equilibria of 5,6,7,8-tetrahydro-4-azabenz[f]indane-1,3,8-triones [10] make it possible to assume the existence of 4-azaindane-1,3-diones in the enol EH, anionic A⁻, betaine AH, and N-protonated enol EH₂ forms depending on the pH of the medium. However, we found that III a-d exist only in the anionic, enol, and protonated enol forms, and the compounds are depicted arbitrarily in the diketo form in the scheme given below. Both alkaline and neutral solutions of these compounds have identical absorption spectra (see Fig. 1 and Table 1) and contain only the anionic form with a characteristic

TABLE 1. Electronic Absorption Spectra of Some 4-Azaindane-1,3-diones

Compound	λ_{max} , nm (log ϵ)					
	anion A ⁻		enol EH		protonated enol EH ₂	
	water	50% ethanol	water	50% ethanol	water	50% ethanol
III b	352 (3,86) 460 (3,25)	357 (3,87) 460 (3,25)	336 (3,66) 406* (2,90)	323 (3,77) 332 (3,77) 406* (3,0)	350 (3,90) 406* (3,23)	351 (3,91) 400-420* (3,3)
III c	362 (3,85) 460 (3,28)	366 (3,86) 463 (3,28)	337 (3,78) 385-420* (2,9)	337 (3,81) 385-420* (3,04)	356 (3,79)	—
III d	378 (4,15) 470* (3,42)	382 (4,19) 470 (3,45)	—	346 (4,1) 445-456 (3,56)	—	385 (4,02)

*Shoulder.

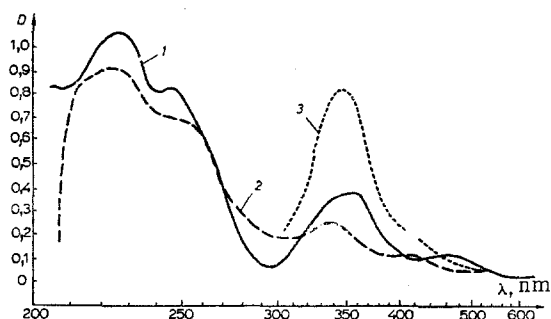
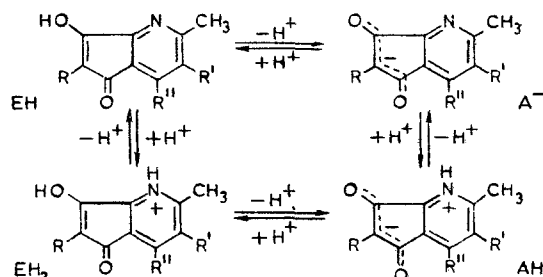


Fig. 1. Electronic absorption spectra of aqueous solutions of IIIb: 1) neutral and 0.5 N KOH; 2) 1.0 N HCl $5 \cdot 10^{-5}$ M; 3) 4.5 N HCl (10^{-4} M).

longwave band at 460–470 nm. In weakly acidic solutions (0.2–1.0 N HCl), which suppress ionization, the enol form with a hypsochromic shift characteristic for it appears. As compared with the 4-azabenzindanedione derivatives that we previously synthesized [10], the inflections at 560–590 or 620–650 nm that are characteristic for the dipolar form of 4-azaindane-1,3-diones are not observed in the case of IIIa–d, and this constitutes evidence for the absence of the betaine form. The equilibrium is shifted to favor the protonated enol in 6 N HCl.

The prototropic transformations of IIIa–d and XVIa,d [10] differ from the transformations of 2-phenyl-4-azaindane-1,3-dione [9], which does not exist in the enol form. The reason for this difference is the reduced basicity of the nitrogen atom of the pyridine ring of IIIa–d and XVIa,d as a result of the electron-acceptor effect of the keto groups.



We calculated the acidity constants (pK_{OH}) in aqueous and 50% aqueous ethanol solutions. It is apparent from Table 2 that the OH acidity increases on passing from the 50% aqueous ethanol solution to an aqueous solution. We were unable to obtain the electronic spectra of aqueous solutions of IIIId and XVIId because of their low solubilities.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer. The electronic absorption spectra were measured with a Specord UV-vis spectrophotometer. The molecular weights were determined with an MKh-1303 mass spectrometer.

3-Amino-2,5-dimethyl-6,7-di(ethoxycarbonyl)-4-azainden-1-one (IVa). A mixture of 4.5 g (0.02 mole) of Ia and 2.6 g (0.02 mole) of IIa was refluxed in 100 ml of absolute ethanol for

TABLE 2. OH-Acidity Constants of IIIb–d and Some Tetrahydro-4-azabenz[f]indane-1,3,8-triones

Compound	pK_{OH}	
	H ₂ O	50% ethanol (by volume)
IIIb	2.93	3.61
IIIc	2.47	2.96
IIId	—	2.61
XVI a [8]	2.84	3.32
XVI d [8]	—	2.39

TABLE 3. Characteristics of the Compounds Obtained

Com- pound	R	R'	mp, °C	Empirical formula	Found, %			Calc., %				Yield, %
					C	H	halo- gen	C	H	halo- gen	N	
IIIa	CH ₃	COOC ₂ H ₅	>250 (dec.)	C ₁₆ H ₁₇ NO ₆ ·1.5H ₂ O	55.4	5.4		55.5	5.8		4.0	30
IIIb	CH ₃	COOC ₃ H ₁₁	230—235 (dec.)	C ₁₈ H ₂₃ NO ₆ ·H ₂ O	60.3	6.1		60.2	6.6		3.7	33
IIIc	CH ₃	CN	>300 (dec.)	C ₁₄ H ₁₂ N ₂ O ₄ ·1.5H ₂ O	55.6	4.5		56.1	5.0		9.4	30
IIId	C ₆ H ₅	COOC ₆ H ₁₁	>300 (dec.)	C ₂₄ H ₂₈ NO ₆ ·H ₂ O	65.0	5.6		65.3	6.2		3.2	24
IVa	CH ₃	COOC ₃ H ₅	140—142	C ₁₆ H ₁₈ N ₂ O ₅	60.4	5.8		60.4	5.7		8.8	9
IVb	CH ₃	COOC ₃ H ₁₁	101—103	C ₁₉ H ₂₄ N ₂ O ₅	63.8	6.7		63.3	6.7		7.8	10
Va	CH ₃	COOC ₃ H ₅	160—165 (dec.)	C ₁₆ H ₁₇ NO ₆ ·HCl	54.2	5.2	10.6	54.0	5.1	10.0	3.9	57
Vb	CH ₃	COOC ₃ H ₁₁	135—140	C ₁₉ H ₂₃ NO ₆ ·HCl	57.5	6.1	8.4	57.4	6.1	8.9	3.5	44
Vc	CH ₃	CN	125—128	C ₁₄ H ₂₁ N ₂ O ₄ ·H ₂ O	57.9	4.5		57.9	4.9		9.6	41
VIa	CH ₃	COOC ₂ H ₅	153—155	C ₁₆ H ₂₀ N ₂ O ₆	57.1	6.0		57.2	6.0		8.3	61
VIIb	CH ₃	COOC ₃ H ₁₁	142—144	C ₁₉ H ₂₆ N ₂ O ₆	60.8	7.0		60.3	6.9		7.4	63
VIIc	CH ₃	CN	179—180	C ₁₄ H ₁₅ N ₃ O ₄	58.0	5.2		58.1	5.2		14.5	56
VId	C ₆ H ₅	COOC ₃ H ₁₁	182—183	C ₂₄ H ₂₈ N ₂ O ₆ ·0.5H ₂ O	64.1	6.6		64.2	6.5		6.2	22
VIIIa	CH ₃	COOC ₃ H ₅	170—175 (dec.)	C ₁₆ H ₁₈ N ₂ O ₅ ·HCl	54.1	5.4	10.3	54.2	5.4	10.3	7.9	45
VIIIa	CH ₃	COOC ₃ H ₅	83—84	C ₁₆ H ₁₈ BrNO ₆	48.3	4.0	19.6	48.3	4.0	20.1	3.5	38
VIIIb	C ₆ H ₅	COOC ₃ H ₁₁	67—70	C ₂₄ H ₂₄ BrNO ₆	57.1	4.9	15.9	57.0	4.8	15.9	2.8	46
IXd	C ₆ H ₅	COOH	>300 (dec.)	C ₁₇ H ₂₁ NO ₆ ·H ₂ O	59.3	3.8		59.5	3.8		4.1	74
XIa	CH ₃	COOH	245—250 (dec.)	C ₁₂ H ₁₀ N ₂ O ₅ ·H ₂ O	51.4	4.4		51.4	4.3		10.0	68
XIIa	CH ₃	COOH	236 (dec.)	C ₁₂ H ₁₀ N ₂ O ₅	55.0	3.9		54.6	3.7		10.6	62
XIVa	CH ₃	COOC ₃ H ₅	150—151	C ₁₆ H ₁₉ NO ₆	60.3	6.0		59.8	6.0		4.4	22

1.5 h, after which the ethanol was removed by distillation, and the residue was dissolved in a small amount of ethyl acetate and chromatographed with a column (3 by 75 cm) filled with Al_2O_3 . The first colored zone was eluted with ethyl acetate to give red crystals (from ethanol). Found: M^+ 318. Calculated: M 318.2. IR spectrum, cm^{-1} : 1568, 1598, 1630, 1645, 1683, 1720, 1742, 3180, 3445.

2,5-Dimethyl-6,7-di(ethoxycarbonyl)-4-azaindane-1,3-dione (IIIa). A second fraction was eluted with ethanol after removal of IVa from the column, and the eluate was evaporated to dryness to give a bright-red substance (from ethanol) that was quite soluble in water but insoluble in nonpolar solvents. IR spectrum, cm^{-1} : 1547, 1557, 1600, 1615, 1677, 1735, 3195, 3394.

3-Amino-2,5-dimethyl-7-ethoxycarbonyl-6-pentyloxycarbonyl-4-azainden-1-one (IVb). The method used to obtain IVa was used to prepare this compound from 2.26 g (0.01 mole) of Ia and 1.57 g (0.01 mole) of IIb. The product was crystallized from aqueous alcohol. IR spectrum, cm^{-1} : 1570, 1600, 1636, 1685, 1730, 3196, 3415.

2,5-Dimethyl-7-ethoxycarbonyl-6-pentyloxycarbonyl-4-azaindane-1,3-dione (IIIb). The method used to prepare IIIa was used to obtain this compound as a bright-red substance (from absolute ethanol). IR spectrum, cm^{-1} : 1530, 1589, 1608, 1651, 1668, 1727, 3270, 3340.

2,5-Dimethyl-7-ethoxycarbonyl-6-cyano-4-azaindane-1,3-dione (IIIc). A mixture of 2.87 g (0.01 mole) of Ia and 0.68 g (0.01 mole) of IIc in 100 ml of absolute ethanol was refluxed for 2 h, after which it was evaporated to 20 ml and chromatographed with a column filled with Al_2O_3 (elution with ethanol). The solvent was evaporated to dryness, and the residue was washed on the filter with ethyl acetate. Two crystallizations from ethanol gave a brick-colored substance. Found: M^+ 272. Calculated: M 272.3. IR spectrum, cm^{-1} : 1553, 1585, 1604, 1674, 1740, 2235 ($\text{C}\equiv\text{N}$), 3415.

5-Methyl-2-phenyl-7-ethoxycarbonyl-6-pentyloxycarbonyl-4-azaindane-1,3-dione (IIId). As in the preparation of diketone IIIa, this compound was obtained from 2.87 g (0.01 mole) of Id and 1.57 g (0.57 mole) of IIb. The structure of the first colored compound obtained by elution from the column with ethanol was not established. Subsequent elution with ethyl acetate gave dark-red crystals (from ethanol). IR spectrum, cm^{-1} : 1533, 1595, 1650, 1718, 3060, 3430.

3-Hydroxy-2,5-dimethyl-6,7-di(ethoxycarbonyl)-4-azainden-1-one Hydrochloride (Va). Concentrated HCl (4 ml) was added to a solution of 0.35 g (1 mmole) of diketone IIIa in 15 ml of glacial acetic acid, and the resulting bright-yellow precipitate was crystallized from dry ethyl acetate. IR spectrum, cm^{-1} : 1617, 1633, 1655, 1680, 1745, 3233, 3452.

3-Amino-2,5-dimethyl-6,7-di(ethoxycarbonyl)-4-azainden-1-one Hydrochloride (VIIa). As in the preparation of hydrochloride Va, this compound was obtained from 0.1 g (0.31 mmole) of enamine IVa, 2 ml of glacial acetic acid, and 8 ml of dilute HCl (1:1) in the form of bright-orange crystals. IR spectrum, cm^{-1} : 1600, 1624, 1645, 1710, 1738, 3130, 3315.

3-Hydroxy-2,5-dimethyl-7-ethoxycarbonyl-6-pentyloxycarbonyl-4-azainden-1-one Hydrochloride (Vb). This compound was similarly obtained from 0.15 g (0.38 mmole) of IIIb, 3 ml of glacial acetic acid, and 10 ml of dilute HCl (1:1) as bright-yellow crystals (from dry ethyl acetate). IR spectrum, cm^{-1} : 1600, 1622, 1732, 3470.

3-Hydroxy-2,5-dimethyl-7-ethoxycarbonyl-6-cyano-4-azainden-1-one (Vc). An 0.3-g (1 mmole) sample of dry diketone IIIc was treated with gaseous HCl until the bright-red starting material was converted to a bright-yellow product (1-2 min). The product was crystallized from dry ethyl acetate. Found: M^+ 272. Calculated: M 272.3. IR spectrum, cm^{-1} : 1554, 1604, 1625, 1695, 1707, 1722, 1738, 3150, 3487.

2,5-Dimethyl-6,7-di(ethoxycarbonyl)-4-azaindane-1,3-dione Ammonium Salt (VIa). Dry ammonia was bubbled into a cooled (cold water) solution of 0.2 g (0.6 mmole) of hydrochloride Va in 25 ml of dry ethyl acetate until the yellow solution turned red (1-2 min). Bright-red salt VIa (from absolute ethanol) precipitated from the solution. IR spectrum, cm^{-1} : 1536, 1590, 1603, 1664, 1705, 1721, 3175, 3320.

2,5-Dimethyl-7-ethoxycarbonyl-6-pentyloxycarbonyl-4-azaindane-1,3-dione Ammonium Salt (VIb). As in the preparation of salt VIa, this salt was obtained from 0.15 g (0.38 mmole) of Vb in the form of bright-red crystals (from absolute ethanol). IR spectrum, cm^{-1} : 1530, 1585, 1600, 1665, 1700, 1720, 3165, 3320.

2,5-Dimethyl-7-ethoxycarbonyl-6-cyano-4-azaindane-1,3-dione Ammonium Salt (VIc). As in the preparation of VIa, this salt was obtained from 0.2 g (0.67 mmole) of Vc and was purified by recrystallization from absolute ethanol. IR spectrum, cm^{-1} : 1534, 1585, 1615, 1652, 1720, 3290.

5-Methyl-2-phenyl-7-ethoxycarbonyl-6-pentyloxycarbonyl-4-azaindane-1,3-dione Ammonium Salt (VID). An 0.44-g sample of diketone IIId was treated with gaseous HCl until the dark-red starting material was converted to a bright-red product (3-4 min). The red, extremely unstable product was immediately dissolved in 50 ml of dry ethyl acetate, the solution was cooled with cold water, and dry ammonia was bubbled into it for 2-3 min. The resulting ammonium chloride was removed rapidly by filtration, and the filtrate was allowed to stand in the cold. The resulting precipitate was crystallized from ethyl acetate and absolute ethanol (6:1). IR spectrum, cm^{-1} : 1515, 1585, 1600, 1645, 1693, 1722, 3086, 3170, 3285.

2-Bromo-2,5-dimethyl-6,7-di(ethoxycarbonyl)-4-azaindane-1,2-dione (VIIIa). A solution prepared from 1 g of bromine and 5 ml of glacial acetic acid was added dropwise to 0.15 g (0.47 mmole) of enamine IVa in 5 ml of glacial acetic acid until the orange reaction mixture turned light yellow. It was then diluted with water and allowed to stand in a refrigerator. Crystals of bromo derivative VIIIa (from aqueous alcohol) precipitated. IR spectrum, cm^{-1} : 1568, 1726, 1748, 1772. A compound identical to VIIIa was similarly obtained from 0.1 g of dione IIIa. The yield of product with mp 84-86° (from aqueous alcohol) was 0.04 g (35.4%). IR spectrum, cm^{-1} : 1570, 1728, 1747, 1772.

2-Bromo-5-methyl-2-phenyl-6,7-di(ethoxycarbonyl)-4-azaindane-1,3-dione (VIIIId). This compound was similarly obtained from 0.25 g (0.47 mmole) of dione IIId. The beige product (from ethanol) dissolved in sodium ethoxide to give a red-brown solution. IR spectrum, cm^{-1} : 1570, 1734, and 1770.

5-Methyl-2-phenyl-4-azaindane-1,3-dione-6,7-dicarboxylic Acid (IXd). An 0.7-g (1.59 mmole) sample of dione IIId was refluxed for 1.5 h in a solution prepared from 0.8 g (0.02 mole) of sodium hydroxide, 50 ml of ethanol, and 20 ml of water. Concentrated HCl was added to the resulting dark-brown solution to give a black precipitate. IR spectrum, cm^{-1} : 1570, 1618, 1715, 1740, 3260, 3520.

5-Methyl-2-phenyl-4-azaindane-1,3-dione-6,7-dicarboxylic Acid Anhydride (Xd). An 0.4-g (1.17 mmole) sample of dry acid IXd was heated at 220° *in vacuo* (15 mm) for 7 h. Workup gave 0.35 g (98%) of black crystals with mp >300° (dec.). IR spectrum, cm^{-1} : 1570, 1630, 1656, 1796, 1841, 1859. Found, %: C 66.5, H 2.6, N 4.2. $\text{C}_{17}\text{H}_9\text{NO}_5$. Calculated, %: C 66.5, H 3.0, N 4.6.

3-Amino-2,5-dimethyl-6,7-di(hydroxycarbonyl)-4-azainden-1-one (XIIa). A solution of 0.2 g of sodium hydroxide in 15 ml of ethanol was added to 0.2 g (0.63 mmole) of enamine IVa in 10 ml of ethanol, after which the mixture was refluxed for 10 min until a bright-orange precipitate formed. The precipitate was removed by filtration and dissolved in 15 ml of water. The solution was neutralized with HCl to give 0.12 g of the bright-red crystal hydrate XIa. IR spectrum, cm^{-1} : 1525, 1590, 1630, 1700, 1720, 3190, 3355.

An 0.12-g (0.43 mmole) sample of crystal hydrate XIa was heated at 180° *in vacuo* (30 mm) for 6 h. The mixture was then worked up to give dark-brown crystals (from ethanol) of XIIa. IR spectrum, cm^{-1} : 1530, 1590, 1640, 1700, 1720, 3190, 3350.

2,5-Dimethyl-6,7-di(ethoxycarbonyl)-4,7-dihydro-4-azaindane-1,3-dione (XIVa). A solution of 0.2 g (1.15 mmole) of sodium hydrosulfite in 10 ml of water was added to a solution of 0.1 g (0.28 mmole) of dione IIIa in 10 ml of water, and the mixture was then stirred at room temperature for 30 min until the orange solution became light yellow. It was then extracted with ethyl acetate (five 50-ml portions), and the ethyl acetate extract was evaporated to 5 ml and chromatographed with a column filled with Al_2O_3 . The eluate was evaporated to dryness to give yellow crystals (from absolute ethanol) that were soluble in sodium methoxide solution to give a red solution. IR spectrum, cm^{-1} : 1518, 1618, 1660, 1684, 1706, 1742, 3000, 3110, 3215, 3252. UV spectrum, λ_{max} , nm (log ϵ) (in neutral solution and in 1 N ethanolic HCl): 251 (4.39) and 391 (3.81); (in 0.05 N ethanolic KOH): 264 (4.42), 380 (3.77), and 494 (3.30).

LITERATURE CITED

1. É. I. Stankevich, A. Ya. Ozola, and G. Ya. Dubur, *Khim. Geterotsikl. Soedin.*, 231 (1975).
2. E. A. Silinsh and L. F. Taure, *Phys. Stat. Sol.*, **2**, 847 (1969).
3. Ya. F. Freimanis, E. A. Silin'sh, O. Ya. Neiland, and L. F. Taure, *Izv. Akad. Nauk Latv. SSR, Ser. Fiz.*, **3**, 28 (1967).
4. A. Ya. Ozola, É. I. Stankevich, and G. Ya. Dubur, *Khim. Geterotsikl. Soedin.*, 1147 (1973).
5. Ya. F. Freimanis and G. Ya. Vanag, *Zh. Obshch. Khim.*, **31**, 1945 (1961).
6. A. Ya. Ozola, É. I. Stankevich, and G. Ya. Dubur, *Khim. Geterotsikl. Soedin.*, 632 (1971).
7. L. É. Neiland, Author's Abstract of Candidate's Dissertation, Riga (1965).
8. L. E. Neiland and G. Vanag, *Khim. Geterotsikl. Soedin.*, 93 (1965).
9. I. V. Turovskii, O. Ya. Neiland, L. É. Neiland, and Ya. P. Stradyn', *Khim. Geterotsikl. Soedin.*, 1382 (1972).
10. O. Ya. Neiland, S. V. Kalnin', É. I. Stankevich, and A. Ya. Ozola, *Khim. Geterotsikl. Soedin.*, 527 (1974).

INVESTIGATION OF NAPHTHYRIDINES.

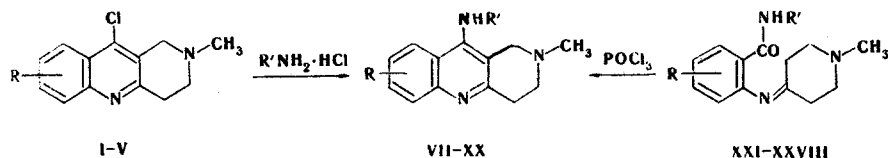
VII.* SYNTHESIS OF 10-ALKYLAMINO-1,2,3,4-TETRAHYDROBENZO[b]-1,6-NAPHTHYRIDINES

V. A. Khaldeeva and M. E. Konshin

UDC 547.836.3

10-Alkylamino-2-methyl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines were obtained by cyclization of alkylamides of N-(1-methyl-4-piperidylidene)anthranilic acids and also by reaction of 10-chloro-2-methyl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines with amine hydrochlorides.

In the present research we attempted to synthesize 10-alkylamino-1,2,2,4-tetrahydrobenzo[b]-1,6-naphthyridines by nucleophilic substitution of the halogen in 10-chloro-2-methyl-1,2,3,4-tetrahydrobenzo[b]-1,6-naphthyridines (I-V) by an alkylamino group.



However, the chlorine in I-V, as in 2,3-polymethylenequinolines [2], proved to have low lability, probably because of the steric and nucleophilic effect of the piperidine ring fused to the quinoline ring. Thus, reaction between benzylamine and I does not occur when they are heated in excess amine at 140° for 7 h, nor when they are heated at 180° for 1 h in phenol. In the latter case we isolated only phenoxy derivative VI.

It is known [3] that the reaction of 4-chloroquinolines with amines is catalyzed by acids; we observed that the corresponding naphthyridines are formed in 16-32% yields in the reaction of amine hydrochlorides with I-V and the hydrochloride of IV with benzylamine (Table 2, method A).

*See [1] for communication VI.