RESEARCH ON 4H-3,1-BENZOXAZINES.

8.* SYNTHESIS AND PROPERTIES OF 4H-3,1-BENZOXAZINIUM CHLORIDES

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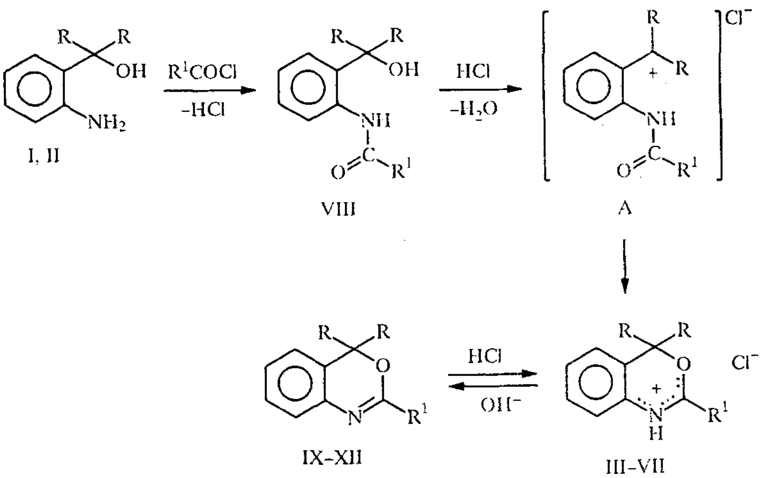
A mechanism for the acylation of substituted o-aminophenylcarbinols with carboxylic acid chlorides and the formation of 2-alkyl(aryl, furyl)-4H-3,1-benzoxazinium chlorides is proposed. The nitration and introduction of a sulfur atom into the heterocyclic ring of the 4H-3,1-benzoxazinium salts were investigated.

We have previously investigated the acylation of o-aminophenyldiphenylcarbinol with carboxylic acid halides in the presence of Lewis acids to give, depending on the reaction conditions, 9-phenylacridinium and 4H-3,1-benzoxazinium salts [1]. In the present research we continued our study of the behavior of tertiary aminophenylcarbinols under the influence of acid chlorides and established that 4H-3,1-benzoxazinium chlorides are formed in this case.



I, III R = CH_3; II, IV—XII R = C_6H_5; III, IV, VIII, IX $R^1 = CH_3$; V, X $R^1 = C_6H_5$; VI, XI R^1 = 2-furyl; VII, XII R^1 = 5-bromo-2-furyl

Acylation of the amino group of starting carbinols I and II in the cold and subsequent dehydration by heating the N-acylamines lead to cations A, which subsequently undergo heterocyclization to salts III-VII. This scheme is confirmed by the synthesis of salt IV from N-acetylamide VIII and is also in agreement with the data in [2, 3].

Excess amounts of the acylating agents were used for the synthesis of the 4H-3,1-benzoxazinium chlorides [1]. Acetyl chloride was used as both the reagent and the solvent to obtain salts III and IV. The synthesis of salts VI and VII was accomplished in chloroform with a twofold excess of the acid chlorides. The use of benzoyl chloride under these conditions

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*For communication 7 see [1].

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TABLE 1. 4H-3,1-Benzoxazinium Chlorides III-VII

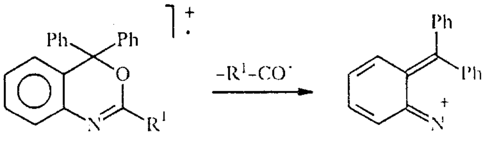
Compound	Empirical formula	mp, °C	IR spectrum, ν, cm^{-1}		Yield, %
			OCNH$^+$	$^+$NH	
III	$C_{11}H_{14}ClNO$	155...156	2450, 1645	1780	65
IV	$C_{21}H_{18}ClNO$	217	2350, 1640	1880	92
V	$C_{26}H_{20}ClNO$	> 200 dec.	2350, 1630	1820	60
VI	$C_{24}H_{18}ClNO_2$	> 220 dec.	2340, 1630	1810	37
VII	$C_{24}H_{17}ClBrNO_2$	177...178	2310, 1650	1800	45

leads to the isolation of 4H-3,1-benzoxazine IX from the reaction medium as a consequence of dehydrochlorination of the salt at the boiling point of the solvent. The synthesis of salt V was therefore accomplished by the reaction of benzoxazine IX with hydrogen chloride.

At room temperature salts III-VI are colorless crystalline substances, and salt VII is yellow; salt V is unstable in air. We ascribe the bands at 1630-1645 cm^{-1} in the IR spectra of the 4H-3,1-benzoxazinium salts (Table 1) to stretching vibrations of an OC$^+$NH fragment, and the vibrational bands at 2310-2450 cm^{-1} and 1780-1880 cm^{-1} constitute evidence for the presence of a quaternized nitrogen atom in the ring. The synthesized salts are readily converted to the corresponding 4H-3,1-benzoxazines in an alkaline medium.

An intense absorption band of a C=N bond at 1625-1635 cm^{-1} is present in the IR spectra of 4H-3,1-benzoxazines IX-XII (Table 2). The UV spectra of 4,4-diphenyl-2-methyl(phenyl, furyl)-4H-3,1-benzoxazines IX-XI are characterized by one absorption maximum at 265-311 nm. In this respect they differ substantially from the spectra of the corresponding dihydrobenzoxazines and the starting carbinols [4]; this is a consequence of the development of an oriented system of π—π conjugation of the aromatic ring with the C=N bond.

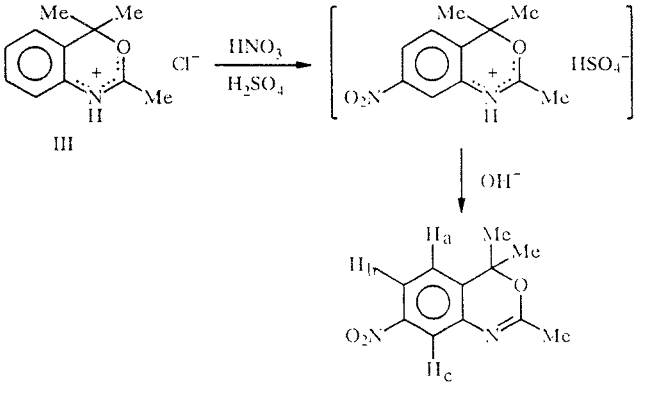
Singly charged M$^+$ molecular ions and a doubly charged M^{++} molecular ion (for IX) are present in the mass spectra of IX, XI, and XII (Table 3). The initial fragmentation of the M$^+$ ions of the 4H-3,1-benzoxazines is characterized by destruction of the heteroring and leads to cation F_1 (m/z 256), which has the maximum intensity [7].



IX, XI, XII

F_1

In the reaction of 2,4,4-trimethyl-4H-3,1-benzoxazinium chloride (III) with a nitrating mixture the heterocyclic ring is retained with attack being directed to the aromatic ring to give 2,4,4-trimethyl-7-nitro-4H-3,1-benzoxazine (XIII).



III

XIII

TABLE 2. 4H-3,1-Benzoxazines and Benzothiazines

Compound	Empirical formula	mp, °C	R_f	UV spectrum, λ_{max}, nm ($\log \varepsilon$)	IR spect. $\nu_{C=N}$, cm^{-1}	Yield, %
IX*	$C_{21}H_{17}NO$	134...135	0,59	265 (4,07)	1635	85
X**	$C_{26}H_{19}NO$	213...215	0,43	303 (4,23)	1620	85
XI***	$C_{24}H_{17}NO_2$	224...226	0,71	311 (4,02)	1630	71
XII	$C_{24}H_{16}BrNO_2$	146...147	0,64	278 (4,15) 328 (3,79)	1625	74
XIV	$C_{21}H_{17}NS$	150...151	0,82	3.06 (3,65)	1620	75
XV	$C_{26}H_{19}NS$	213	0,87	316 (4,18)	1550	82
XVI	$C_{24}H_{17}NOS$	167...168	0,89	310 (4,02)	1570	35
XVII	$C_{24}H_{16}BrNOS$	170...171	0,91	318 (4,13)	1580	42

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*The constants are in agreement with those in [5].

**The constants are in agreement with those in [6].

***The constants are in agreement with those in [1].

TABLE 3. Mass Spectra of 4H-3,1-Benzoxazines

Compound	m/z (I_{rel}, %)*
IX	299 (29), 275 (35), 256 (100), 202 (16), 180 (22), 165 (13), 149 (22), 85 (26), 69 (26), 60 (32), 57 (49)
XI	351 (76), 322 (13), 256 (100), 254 (26), 193 (24), 191 (21), 95 (71), 83 (34), 75 (42), 73 (82), 60 (53)
XII**	429 (25), 350 (47), 322 (11), 266 (100), 254 (25), 239 (7), 173 (19), 165 (6), 152 (6), 95 (3), 77 (8)

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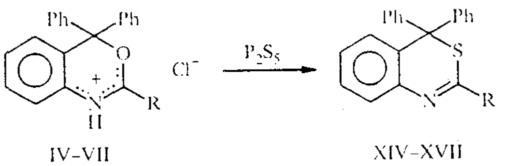
*The M^+ peaks and the 10 most intense peaks are presented.

**The m/z values of the M^+ ions were calculated on the basis of the light isotope of the halogen (^{79}Br).

The PMR spectrum of XIII contains signals of the vicinal H_a and H_b aromatic protons with a spin-spin coupling constant (SSCC) of 9 Hz and of the H_c proton in the form of a doublet with $^4J_{bc}$ = 3 Hz, which is in agreement with the data in [8].

In order to introduce new heteroatoms into the heteroring of the benzazine system we fused 4H-3,1-benzoxazinium salts IV-VII at 170-210°C with phosphorus pentasulfide [9].



IV-VII XIV-XVII

XIV R = CH_3; XV R = C_6H_5; XVI R = 2-furyl XVII R = 5-bromo-2-furyl

Salts VI and VII, which contain a furan ring, resinified under the conditions of the method in [9]. We found that it was possible to obtain furan-containing benzothiazines in the form of bases XVI and XVII by refluxing the starting salts in benzene. In the IR spectra of benzothiazines XV-XVII (see Table 2) the characteristic absorption band of a C=N bond undergoes a bathochromic shift as compared with the vibrations of the same bond in 4H-3,1-benzoxazines.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds at room temperature were recorded with a Specord IR-75 spectrometer. The mass spectra were obtained with Varian MAT CH-6 and LKB-2091 spectrometers by direct introduction of the substances into the ion source at an ionization energy of 70 eV at 70°C and 100°C. The electronic spectra of solutions in ethanol were recorded with a Specord UV-vis spectrophotometer. Thin-layer chromatography was carried out in a benzene—ether system (8:2) on Silufol UV-254 plates with development by iodine vapors. Silica gel (L40/100) was used for column chromatography.

The results of elemental analysis of the synthesized compounds for C, H, Cl, and N were in agreement with the calculated values.

2-Methyl-4,4-diphenyl-4H-3,1-benzoxazinium Chloride (IV). A 1.37-g (0.005 mole) sample of o-aminophenyldiphenylcarbinol was added gradually with stirring and cooling (ice bath) to 15 ml of acetyl chloride, and the reaction mixture was heated on a water bath until the solid material vanished. The mixture was then cooled, and the salt was precipitated with absolute ether to give 1.55 g (92%) of product IV.

Salt III was similarly obtained using o-aminophenyldimethylcarbinol [4].

2,4,4-Triphenyl-4H-3,1-benzoxazinium Chloride (V). Dry hydrogen chloride was passed through a solution of 1 g (0.0028 mole) of 2,4,4-triphenyl-4H-3,1-benzoxazine (X), obtained by the method in [1], in 10 ml of absolute ether. The resulting precipitate was removed by filtration and transferred rapidly to an isolation chamber. The yield was 0.67 g. The product should be stored in a sealed ampul.

2-Furyl-4,4-diphenyl-4H-3,1-benzoxazinium Chloride (VI). A 1.37-g (0.005 mole) sample of o-aminophenyldiphenylcarbinol was added with stirring to a cooled (to 0°C) solution of 1.3 g (0.01 mole) of pyromucic acid chloride in 10 ml of chloroform, and the reaction mixture was heated for 30 min up to the boiling point of chloroform. The resulting precipitate gradually vanished. The solution was cooled, and the product was precipitated with ether and removed by filtration. The yield was 0.72 g.

Salt VII was similarly obtained.

2-Methyl-4,4-diphenyl-4H-3,1-benzoxazine (IX). A 3.35-g (0.01 mole) sample of salt IV was mixed with 25 ml of 5% $NaHCO_3$ solution, and the mixture was stirred for a few minutes at room temperature. The precipitate was removed by filtration. The yield of the product was 2.55 g. Benzoxazines XI and XII were similarly obtained.

2,4,4-Trimethyl-7-nitro-4H-3,1-benzoxazine (XIII, $C_{11}H_{12}N_2O_3$). A 0.125-ml (0.003 mole) sample of nitric acid (d = 1.5) was added with cooling (ice bath) to a mixture of 0.5 g (0.0024 mole) of chloride III in 4 ml of concentrated H_2SO_4 (d = 1.84), after which the mixture was allowed to stand in a refrigerator for 72 h. It was then poured over crushed ice, and the aqueous mixture was neutralized with 10% $NaHCO_3$ solution. A yellow precipitate formed when the mixture was slightly alkaline. It was removed by filtration and washed with water. The yield of the product with mp 76-77°C and R_f 0.43 was 0.35 g (67%). UV spectrum: λ_{max} 320 nm (log ε 4.01). IR spectrum: 3030, 1640 (C=N); 1530, 1350 cm^{-1} (NO_2). PMR spectrum (in $CDCl_3$): 1.62 [6H, s, 4-$(CH_3)_2$], 2.11 (3H, s, 2-CH_3), 7.25 (1H, d, $^3J_{ab}$ = 9 Hz, H_a), 7.90 (1H, d, $^4J_{bc}$ = 3 Hz, H_c), and 8.15 ppm (1H, t, $^4J_{bc}$ = 9 Hz, $^3J_{ab}$ = 3 Hz, H_b).

2-Furyl-4,4-diphenyl-4H-3,1-benzothiazine (XVI). A mixture of 0.78 g (0.002 mole) of chloride VI and 0.45 g (0.002 mole) of P_2S_5 in 15 ml of absolute benzene was refluxed for 2 h, after which it was cooled, and the benzene solution was removed by filtration and concentrated. The resulting crystals were purified by column chromatography. The yield was 0.26 g.

Compounds XIV-XVII were similarly obtained.

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