BENZOXAZINES AND RELATED COMPOUNDS

II. Synthesis of 2-Substituted 4, 4-Dialkyl-4H-1, 3-Benzoxazines. *

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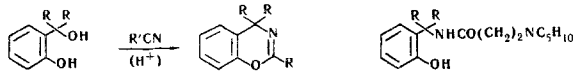
A simple method has been elaborated for synthesizing 2-substituted 4, 4-dialkyl-4H-1, 3-benzoxazines by the interaction between nitriles and o-oxyphenyldialkylcarbinols under the influence of acids.

Previously on studying the reaction between acetonitrile and o-oxyphenyldialkylcarbinols under the influence of acids in separate examples we established the formation of cyclic products, 2-methyl-4, 4-dialkyl-4H-1, 3-benzoxazines. Considering that the 4, 4-dialkyl-4H-1, 3-benzoxazines have remained essentially uninvestigated to the present time, we synthesized a number of this type of compounds by the above-mentioned method.

o-Oxyphenyldiethylcarbinol and o-oxyphenyldimethylcarbinol were used as the carbinol component, and from the nitriles acrylonitrile, chloracetonitryl, benzylcyanide, p-chlorobenzonitryl, the cyanoacetic ester, the cyanhydrin of acetone, and the nitrile of ω-piperidinoenanthic acid (**XI**) were used.

The reaction was conducted either in the presence of 70% perchloric acid, or in a mixture of sulfuric and acetic acids. The benzoxazines **I–VII** and **IX** are colorless liquids. The C=N bond is characteristic in the IR spectrum with frequencies in the region of 1700 cm^{-1}.



IX R=CH_3; I–VIII C_2H_5; I R′=CH=CH_2; II R′=CH_2Cl; III R′=$CH_2C_6H_5$; IV R′=*p*-ClC_6H_4; V R′=$CH_2COOC_2H_5$; VI R′=$(CH_3)_2C(OH)$; VII R′=$(CH_2)_6NC_5H_{10}$; VIII R′=$(CH_2)_2R''$, where R″ = 4,4-diethyl-4H-1,3-benzoxazinyl-2; IX R′ = CH_3

It was found impossible to obtain the corresponding benzoxazine using β-piperidinopropionitrile. The reaction proceeded slowly in perchloric acid and in a mixture of sulfuric and acetic acids in addition to the product of the normal Ritter reaction, N-(β-piperidinopropionyl)-α, α-diethyl-o-oxybenzilamine (**X**), the vinylbenzoxazine of compound I was formed as a result of β-elimination of piperidine. Amides with a type **X** open chain may be obtained in other instances, and thus in order to synthesize benzoxazines it is important to select conditions in which the formation of such amides as the unsaturated compounds (oxystirols) from carbinols would be suppressed.

EXPERIMENTAL

2-Vinyl-4, 4-diethyl-4H-1, 3-benzoxazine (I). A 5 ml volume of 70% perchloric acid was added dropwise to a mixture of 5.4 g (0.03 mole) of o-oxyphenyldiethylcarbinol [1] and 5.3 g (0.1 mole) of acrylonitrile cooled to 0° C at such a rate that the temperature of the reaction mixture was from 0–10° C. After 24 hr, the reaction mass was made alkaline with aqueous ammonia and extracted with ether. The ethereal extracts were dried with magnesium sulfate, and the ether was removed by distillation and compound I was sublimated under vacuum. IR spectrum: $\nu C{=}N$ 1678 cm^{-1}.

The benzoxazines of compounds **II**, **III**, **V**, **VI**, and **IX** (see table) were obtained in an analogous manner.

*For part I, [1].

2-(6-Piperidinohexyl)-4, 4-diethyl-4H-1, 3-benzoxazine (VII). A 5 ml volume of conc H_2SO_4 was added dropwise to a mixture of 5.4 g (0.03 mole) o-oxyphenyldiethylcarbinol and 6 g (0.03 mole) of the nitrile of ω-piperidinoenanthic acid (XI) in 15 ml of glacial acetic acid at such a rate that the temperature of the reaction mixture was 40–50° C. Subsequent treatment was conducted as described for compound **I.**

2-Substituted 4, 4-Dialkyl-4H-1, 3-benzoxazines (I–IX)

Compound	Bp °C (pressure, mm)	n_D^{22}	Empirical formula	Found, %			Calculated, %			Yield, %
				C	H	N	C	H	N	
I	83—84 (1)	1.5330	$C_{14}H_{17}NO$	77.7; 77.8	7.9; 7.9	6.5; 6.4	78.1	8.0	6.5	40
II	106—107 (1)	1.5315	$C_{13}H_{16}NOCl$	Cl 14.6; 14.8	—	6.0; 6.1	Cl 15.0	—	6.1	32
III	116—117 (0.03)	1.5560	$C_{19}H_{21}NO$	82.0; 82.2	7.6; 7.7	5.3; 5.4	81.7	7.6	5.0	57
IV	153—154 (0.03)	1.5800	$C_{18}H_{18}NOCl$	72.2; 72.3	6.0; 6.1	11.6; Cl 11.5	72.1	6.0	Cl 11.8	46
V	109—110 (0.06)	1.5175	$C_{16}H_{21}NO_3$	69.8; 70.1	7.7; 7.7	5.0; 5.1	69.8	7.7	5.0	32
VI*	118—119 (4)	1.5050	$C_{15}H_{21}NO_2$	—	—	5.7; 5.6	—	—	5.7	86
VII	178—179 (0.2)	1.5160	$C_{23}H_{36}N_2O$	77.2; 77.1	10.0; 10.2	7.9; 7.7	77.5	10.2	7.8	41
VIII	—**	—	$C_{26}H_{32}N_2O_2$	77.1; 77.3	8.1; 8.2	7.2; 7.3	77.2	8.0	6.9	50
IX	83—84 (4)	1.5229	$C_{11}H_{13}NO$	75.2; 75.2	7.5; 7.5	8.0; 7.8	75.4	7.5	8.0	22***

*Hydrochloride of VI (from an ethereal solution of VI by the action of hydrogen chloride), mp 167.5-168.5° C. Found, % C 63.2, 63.3; H 7.8, 7.8; Cl 12.7, 12.7. Calculated for $C_{15}H_{21}NO_2 \cdot HCl$, %: C 63.5; H 7.8; Cl 12.5;

**Mp 138.5-139° C

***In addition to compound IX significant quantities of a substance with a mp of 102-103° C are found. The structure of this compound is being elucidated.

The benzoxazines of compound IV and VIII (table) were obtained in an analogous manner.

Nitryl of ω-piperidinoenanthic acid (XI). A 17.5 g (0.12 mole) quantity of the nitrile of ω-chloroenanthic acid [2] was boiled for 10 hr with 20.4 g (0.24 mole) of piperidine in 100 ml of xylol. After cooling, the precipitate was removed by filtration, the solvent was distilled off, and the residue was sublimed under vacuum. A 12.5 g (23.3%) quantity of compound **XI** was obtained with a bp of 134–136° C. (2 mm); n_D^{22}, 1.4691; Found, %: C 74.3, 74.0; H 11.6, 11.6; N 14.4, 14.3. Calculated for $C_{12}H_{22}N_2$, %: C 74.2; H 11.4; N 14.4.

Reaction between o-oxyphenyldiethylcarbinol and β-piperidinopropionitrile. A 8 ml volume of conc H_2SO_4 was added to a mixture of 4 g (0.022 mole) of o-oxyphenyldiethylcarbinol and 4.83 g (0.035 mole) of piperidinopropionitryl in 50 ml of acetic acid with stirring at such a rate that the temperature of the reaction mixture was 40–50° C. After 24 hr the reaction mass was poured onto ice, the acid solution was washed with ether, and made alkaline with aqueous ammonia and the separated oil was extracted with ether. The ethereal extracts were dried with magnesium sulfate, the ether was removed by distillation, petroleum ether was added to the residue, the resulting crystals were removed by filtration and recrystallized from n-heptane. A 2.05 g (29%) quantity of compound **X** was obtained with a mp of 101–101.5° C. Found, %: C 71.7, 71.6; H 9.5, 9.6; N 9.0, 9.2. Calculated for $C_{19}H_{30}N_2O_2$, %: C 71.6; H 9.5; N 8.8. IR spectrum, cm^{-1} (in $CHCl_3$, c 0.78%, d 0.06 mm): 1667 (amide of I), 1570 (amide of II) a wide band in the 3400–3200 region. Petroleum ether was distilled off, the residue was sublimed under vacuum, and the fraction with a bp of 135–140° C (5 mm) was collected. A solution of this fraction in ether was washed with 15% HCl, and then water. Compound **I** with a bp of 137–138° C (5 mm) was extracted from the ethereal solution by sublimation. The substance was identical in relation to the IR spectrum to the sample obtained as shown above.

REFERENCES

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