UNSATURATED 3-ACYLBENZOXAZOLINONES — DIENOPHILES IN DIENE SYNTHESIS REACTIONS. I

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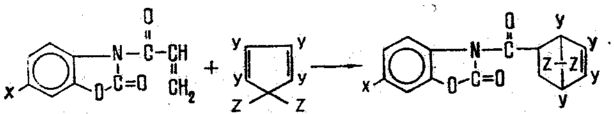
It has been shown that unsaturated 3-acylbenzoxazolinones readily take part in reactions with cyclopentadienes and give good yields of the corresponding 3-(bicyclo[2,2,1]hept-5-ene-2-carbonyl)benzoxazolinones.

Benzoxazolinone and compounds related to it have been isolated from a dry powder of the roots of *Scoparia dulcus* [1]. This plant has long been used in Eastern folk medicine in diabetes and also in hypertonic disease. According to available information [2], 6-methoxybenzoxazolinone is an inhibitor of the growth of the roots of certain plants.

In view of the synthetic availability of benzoxazolinone, we have made a systematic search for biologically active substances in this series of compounds [3]. In the present paper we consider the dienophilic activity of unsaturated alkylbenzoxazolinones in the Diels-Alder reaction and the pesticidal properties of the adducts obtained. The reactions have been studied of 3-acryloylbenzoxazolinone (I), 3-acryloyl-6-chlorobenzoxazolinone (II), and 3-acryloyl-6-bromobenzoxazolinone (III) [3] with a number of dienes, as which we used cyclopentadiene (IV), hexachlorocyclopentadiene (V), tetrachlorocyclopentadiene (VI), and tetrachloro-5,5-dimethoxycyclopentadiene (VII).

A characteristic feature of (IV) is the case with which it takes part in the diene synthesis [4]. This property is due to the fact that the molecule of (IV) and its derivatives, in contrast to acyclic dienes, has a system of conjugated double bonds fixed in the "cisoid" position which is the most favorable for the performance of the Diels-Alder reaction.

On this basis we have studied the condensation of the 3-acryloylbenzoxazolinones (I-III) with the dienes (IV-VII), which are represented in general form in Scheme 1.



I-III IV-VII VIII-XI a,b,c

VIIIa X=H, Y=H, Z=H; VIIIb X=Cl, Y=H, Z=H; VIIIc X=Br, Y=H, Z=H; IXa X=H, Y=Cl; IXb X=Cl, Y=Cl, Z==Cl; IXc X=Br, Y=Cl, Z=Cl; Xa X=H, Y=Cl, Z=H; Xb X=Cl, Y=Cl, Z=H; Xc X=Br, Y=Cl, Z=H: XIa X=H, Y=Cl, $Z=OCH_3$; XIb X=Cl, Y=Cl, $Z=OCH_3$; XIc X=Br, Y=Cl, $Z=OCH_3$.

Scheme 1

To obtain higher yields of the reaction products we varied the conditions of performing the synthesis: the molar ratio, the temperature, and the time (Table 1). Thus, the reaction of 3-acryloylbenzoxazolinone with the diene (IV) at a ratio of dienophile to diene of 1:10 at a reaction temperature of 40-41°C for 7 h led to the adduct — 3-(bicyclo[2,2,1]hept-5-ene-2-carbonyl)benzoxazolinone (VIIIa) — in practically quantitative yield. The diene condensation of the 6-substituted 3-acryloylbenzoxazolinones with (IV) at the boiling point of the

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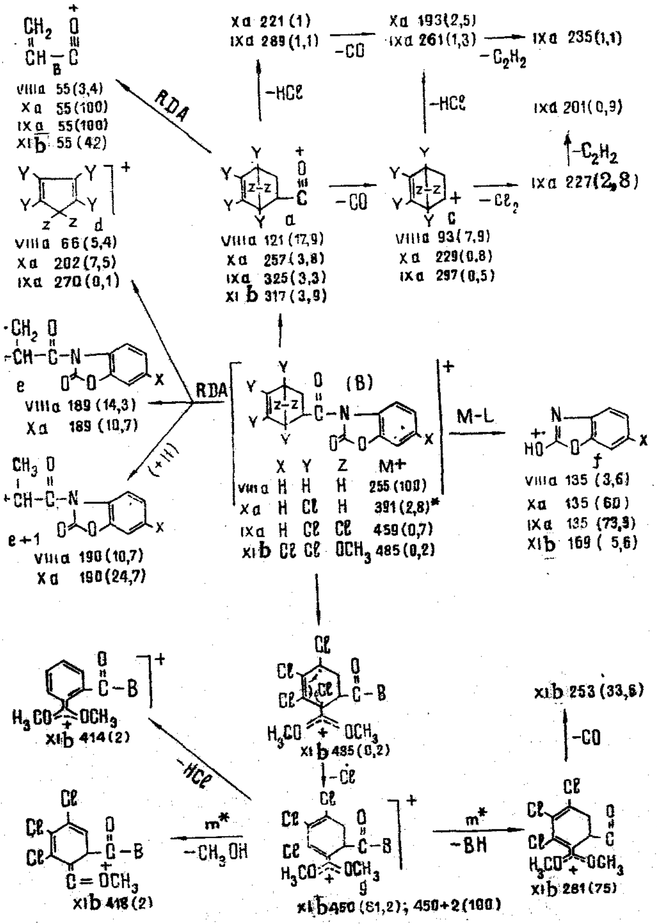
reaction mixture with a molar ratio of acryloylbenzoxazolinone to (IV) of 1:10 took place fairly readily with the production of high yields of (VIIIb and c).

It is known that hexachlorocyclopentadiene (V) is a fairly active diene capable of reacting with various dienophiles [5, 6] and it was therefore of interest to study the reaction of diene (V) with (I-III). It was found that it takes place in toluene solution at 105-110°C in 12 h with the formation of 3-(1,4,5,6,7,7-hexachlorobicyclo[2,2,1]hept-5-ene-2-carbonyl)-benzoxazolinone.

The performance of the reaction at higher temperatures, just as with an increase in the amount of (V) ((V): (I) = 3:1), led to a fall in the yield of product. Under similar conditions the reaction of acryloylbenzoxazolinones with the incompletely chlorinated diene (VI) gave good yields of the 3-(1,4,5,6-tetrachlorobicyclo[2,2,1]hept-5-ene-2-carbonyl)benzoxazolinones (Xa-c). The normal adducts (XIa-c) were also formed by the condensation of tetrachloro-5,5-dimethoxycyclopentadiene (VII) with the dienophiles (I-III). The reaction took place in solution (toluene) at the boiling point of the reaction mixture for 8-12 h.

The results obtained (Table 1) show that the introduction of electronegative atoms (Cl, Br) into position 6 of 3-acryloylbenzoxazolinone lowers the dienophilic activity of the latter. Apparently, the substituents partially lower the electron density on the oxygen atom of the acryloyl fragment through the conjugation of the benzene ring and the unshared pair of electrons of the nitrogen atom; however, both the unsubstituted 3-acryloylbenzoxazolinone and its 6-substituted analogs are good dienophiles and react readily with cyclopentadiene and its substituted derivatives.

The structures of the compounds synthesized were confirmed by a study of their fragmentation pathways on mass spectroscopy (Scheme 2).



Scheme 2. *The mass of the ion shown relates to the ^{35}Cl isotope.

TABLE 1

Diene	Di-enophile	Ratio of diene to dienophile	Solvent	Temperature, °C	Time of the reaction, h	mp of the adduct, °C	R_f	Yield of the adduct, %	Empirical formula	Elementary analysis					
										found, %			calculated, %		
										C	H	N	C	H	N
IV	I	2:1	—	40—41	7	125—127	0,90	15	$C_{15}H_{13}NO_3$	70,18	5,29	5,29	70,58	5,09	5,09
IV	I	5:1	—	"	"	"	"	40	"						
IV	I	10:1	—	"	"	"	"	95	"						
IV	II	10:1	—	"	"	136—137	0,92	90	$C_{15}H_{12}NO_3Cl$	62,42	5,40	4,73	62,80	5,10	4,83
IV	III	10:1	—	"	"	149—150	0,92	88	$C_{15}H_{12}NO_3Br$	53,50	3,19	4,53	53,89	3,59	4,19
V	I	1,1:1	Xylene	130—140	12	116—117	0,93	50	$C_{15}H_7NO_3Cl_6$	38,79	2,05	3,36	38,96	1,52	3,03
V	I	1,1:1	Toluene	105—110	"	"	"	63	"						
V	I	3:1	"	"	"	"	"	55	"						
V	II	1,1:1	"	"	"	151—153	0,97	45	$C_{15}H_6NO_3Cl_7$	36,36	1,55	2,77	36,25	1,21	2,82
V	III	1,1:1	"	"	"	149—150	0,95	55	$C_{15}H_6NO_3Cl_6Br$	33,30	1,50	2,66	33,27	1,10	2,57
VI	I	1:1	"	"	7	133—135	0,91	64	$C_{15}H_9NO_3Cl_4$	46,41	2,19	3,94	45,8	2,28	3,55
VI	I	"	"	"	12	"	"	80	"						
VI	II	"	"	"	"	162—164	0,93	76	$C_{15}H_8NO_3Cl_5$	42,62	2,02	3,94	42,10	1,87	3,27
VI	III	"	"	"	"	175—180	0,94	66	$C_{15}H_8NO_3Cl_4Br$	37,94	1,43	2,84	38,13	1,69	2,96
VII	I	1,1:1	"	"	8	137—139	0,96	77	$C_{17}H_{13}NO_5Cl_4$	46,87	3,15	3,50	47,24	2,88	3,09
VII	I	"	"	"	12	"	"	78	"						
VII	II	"	"	"	8	185—186	0,93	76	$C_{17}H_{12}NO_5Cl_5$	41,67	2,30	2,86	41,84	2,46	2,87
VII	III	"	"	"	"	180—185	0,94	69	$C_{17}H_{12}NO_5Cl_4Br$	37,85	2,49	2,70	38,15	2,25	2,63

Scheme 2 shows the fragmentation pathways of compounds (VIIIa), (IXa), (Xa), and (XIb), which are adducts of dienes and dienophiles, since substituents at C_6 in the benzoxazolinone ring, apart from changing the mass numbers of the fragments, do not affect the course of fragmentation under electron impact.

Thus, in the mass spectra of (VIIIa), (IXa), (Xa), and (XIb) α-cleavage from the C=O group takes place which leads to bicyclo[2,2,1]hept-5-ene-2-carbonyl cations (a), and then these ions form by a retrodiene decomposition mechanism the acryloyl ion (b) with m/e 55 and, in addition, with the splitting out of a C=O molecule they are transformed into bicyclo[2,2,1]hept-5-ene ions (c). The further decomposition of ions *a* and c was followed in the spectra of (IXa) and (Xa), and took place through the elimination of molecules of HCl and of Cl_2 and then, in the case of (IXa) only, of C_2H_2.

The breakdown of the molecular ions by the retrodiene process [7] leads to the ions of cyclopentadiene (d) (VIIIa, IXa, Xa) and of 3-acryloylbenzoxazolinone (e) (VIIIa, Xa), while the migration of one hydrogen atom gives rise to the protonated form of the ion e (e + 1), as is confirmed by the appearance of a m^+ peak.

The fragmentation of the M^+ ions of (VIIIa, IXa, Xa, and XIb) by means of a McLafferty rearrangement [8] reduces ions of 2-hydroxybenzoxazole (f) while the H from C_2 of the bicyclic fragment passes to the oxygen (C=O) of the benzoxazolinone.

In the spectra of the chlorine-substituted bicyclic fragments the elimination of a chlorine atom is observed. This process takes place very actively in the case of the 7,7-dimethoxy derivatives (XI) which is obviously connected with the presence of two OCH_3 groups at C_7 upon which a positive charge may readily be localized, and therefore this fragmentation pathway dominates over the other processes. The mechanism of the ejection of Cl can be followed in Scheme 2 on the basis of the formation of the ion g. Then, in the spectrum of (XIa), by the splitting out of molecules of HCl, CH_3OH, and benzoxazolinone, ion g is converted into ions with m/e 414, 418, and 281 and the latter, in its turn, by eliminating a molecule of CO, forms an ion with m/e 253.

Thus, as the result of the investigation of the fragments of the compounds synthesized it has been possible to show their structure. The M^+ ions of the compounds obtained form bicyclo[2,2,1]hept-5-ene-2-carbonyl ions which then decompose by a retrodiene mechanism.

It was found that the 1,4,5,6-tetrachloro-7,7-dimethoxy derivatives fragment with the elimination of a chlorine radical.

The IR spectra of the compounds studied show a shift of the absorption band of the C=O group of the oxazole ring by 10-30 cm^{-1}.

The UV spectra of compounds (IXa, b) in ethanol have two absorption maxima — one in the shortwave region at 214-216 mμ, and the second in the long-wave region at 260 mμ — which are characteristic for this class of compounds. In an alkaline medium at pH 11, in the case of (VIII, IXa and b, and XI) these absorption maxima undergo a bathochromic shift to 248 and 290 mμ, respectively. The compounds probably split as the result of hydrolysis with the formation of benzoxazolinone. In an acid medium at pH 1 the spectra of these compounds (VIII, IXa and b, and XI) are identical with their spectra in C_2H_5OH (Fig. 1).

The UV spectrum of compound (Xb) in ethanol has three absorption maxima; the first at 210 mμ (log ε 4.27), the second expressed in the form of a plateau at 255 mμ (log ε 3.78), and the third at 285 mμ (log ε 3.84). In an acid medium the 255 mμ maximum undergoes a hypsochromic shift to 230 mμ, while the last one remains unchanged. In an alkaline medium a well-defined maximum appears at 248 mμ with a higher intensity of absorption than the maximum at 255 mμ, and a small bathochromic shift of the absorption band at 285 mμ to 292 mμ takes place.

Particular interest is caused by the spectrum in ethanol of compound (XIa) in which there are methoxy substituents in the bicyclic system. It has its first absorption maximum at 202 mμ (log ε 4.50) in place of the 214-216 mμ for compounds (IXa and b) and a second maximum at 280 mμ, less well defined than that at 202 mμ, with log ε 3.84 and having a small vibrational structure.

The pattern of the spectrum changes sharply in an acid medium at pH 1 — the absorption band at 280 mμ disappears completely and the first absorption maximum at 202 mμ passes into a broad diffuse plateau up to 230 mμ.

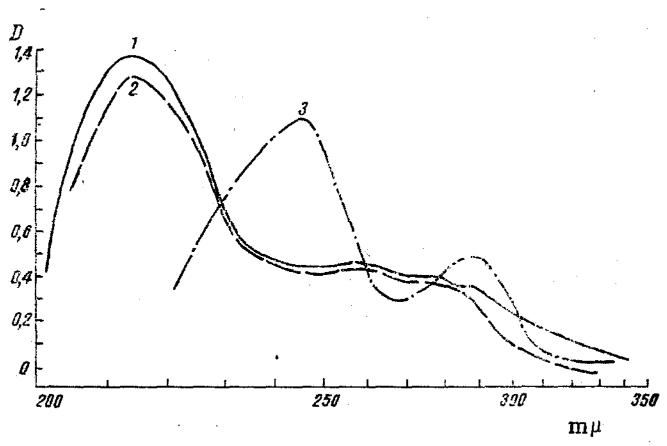


Fig. 1. UV spectra of (IXa and b): 1) in C_2H_5OH; 2) in an acid medium; 3) in an alkaline medium.

Thus, the UV spectra of the compounds studied are characteristic for the series of the substances and can be used for their identification.

The compounds synthesized exhibited a weak pesticidal activity.

EXPERIMENTAL

The purity of the compounds synthesized was checked by thin-layer chromatography on Silufol plates using the benzene–ethanol (10:1) system.

IR spectra were taken on a UR-20 instrument (tablets with KBr), UV spectra on a Specord UV-VIS spectrophotometer, and mass spectra on MKh-1303 instrument at a temperature of the inlet tube of 120-130°C with an ionizing voltage of 40 V. The results of determination of elementary composition agreed with the calculated figures.

Synthesis of 3-(Bicyclo[2,2,1]hept-5-ene-2-carbonyl)benzoxazolinone (VIIIa). A three-necked flask was charged with 1.89 g (0.01 mole) of 3-acryloylbenzoxazolinone (I) and a small amount of hydroquinone. With stirring, 6.6 g (0.10 mole) of freshly-prepared cyclopentadiene (IV) was added, and then the reaction mixture was heated at 40-41°C for 7 h. After the excess of (IV) had been distilled off, the residue was dissolved in acetone and precipitated with water. The crystals that deposited were filtered off and were recrystallized from isooctane. This gave 2.42 g (95% of theory) of the adduct (VIIIa) with mp 125-127°C; R_f 0.90 [benzene–ethanol (10:1)]. (For characteristics of the mass spectrum, see above). The structure of (VIIIa) was studied by hydrolysis with a 4% aqueous solution of caustic soda, as a result of which we isolated benzoxazolinone (mp 135°C, R_f 0.30) and bicyclo[2,2,1]hept-5-ene-2-carboxylic acid (bp 132-134°C/20 mm, R_f 0.40).

Compounds (VIIIb and c) were synthesized from the appropriate dienes and dienophiles under the conditions of obtaining (VIIIa) (Table 1).

Synthesis of (1,4,5,6,7,7-Hexachlorobicyclo[2,2,1]hept-5-ene-2-carbonyl)benzoxazolinone. With stirring, 1.89 g (0.01 mole) of compound (I) containing traces of hydroquinone was dissolved in 30 ml of dry toluene. To the resulting solution 3 g (0.011 mole) of (V) was added dropwise, and then the reaction mixture was heated at 110-115°C for 12 h. After the toluene had been distilled off, the residue was recrystallized from isooctane, which gave 2.9 g (63% of theory) of the adduct (IXa) with mp 116-117°C, R_f 0.97.

The adducts (IXa-c, Xa-c, and XIa-c) were obtained from the appropriate dienophiles and dienes under the conditions described (Table 1). Compounds (VI) and (VII) were synthesized as described in the literature [9, 10].

SUMMARY

Unsaturated 3-acylbenzoxazolinones are good dienophiles and readily react with cyclopentadiene and its derivatives.

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