11. V. D. Orlov, A. I. Roberman, and I. A. Fedyunyaeva, Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol., 25, 675 (1982).
12. N. A. Izmailov, Electrochemistry of Solutions [in Russian], Izd. Khar'kovsk. Univ., Khar'kov (1959), p. 665.
13. T. V. Mozharova, Candidate's Dissertation in Chemical Sciences, Khar'kov (1967), p. 8.
14. T. Kimura, T. Kai, and N. Tasuoka, Acta Crystallogr., 33, 1786 (1977).

SYNTHESIS OF N-CARBOXYLALKYLBENZIMIDAZOLIN-2-ONES

S. S. Khalikov, Ch. Sh. Kadyrov, A. T. Ayupova, and L. V. Molchanov

UDC 547.785.5:542.951.1:632.9.52

The corresponding N-mono- and N,N'-dicarboxylalkylbenzimidazolin-2-ones were prepared by the reaction of the sodium salts of benzimidazolin-2-one and its 1,5,6-substituted derivatives with chloroacetic acid, acrylonitrile, and γ-butyrolactone.

N-Alkyl-substituted benzimidazolin-2-ones are of interest as potential pesticides: they include substances which have growth-regulating [1] and fungicidal [2, 3] properties. Benzimidazolyl-N-acetic acid also exhibits some auxin activity [4]. The activity of these compounds could be explained by concepts of the mechanism of β-oxidation [5], where arylhydroxycarboxylic acids with an odd number of methylene groups can be transformed into active acetic acid homologs, while acids with an even number of methylene groups yield phenols, which have no growth-stimulating activity.

We synthesized N-carboxylalkylbenzimidazolin-2-ones (IIa-f–IVa-f) and studied the conditions of the reaction of the sodium salts of benzimidazolin-2-ones (Ia-f) with halogenated aliphatic acids (chloroacetic, α-chloro- and β-bromopropionic, and β-chlorobutryic) to determine the effect of the length of the carboxylalkyl substituent on the manifestation of pesticidal activity and the basicity of benzimidazolin-2-ones during the reaction of N-carboxylalkylation.

The products of carboxylalkylation of IIa-f (Table 1) could only be obtained with chloroacetic acid after modification of the conditions in [6]. In N-alkylation of compound Ie with bromoacetic acid ethyl ester in a solution of sodium ethylate [7], 1-carboxymethylbenzimidazolin-2-one ethyl ester was separated. However, in the alkylation of compounds Ie and f with chloroacetic acid, the isopropenyl group is preserved, and the corresponding 1-isopropenyl-3-carboxymethyl derivatives of IIe and f were obtained, which form benzimidazolin-2-ones IIg, h. Unsubstituted in position 1(3).

The negative results in the carboxylation of benzimidazolin-2-one salts Ia-f by other halogenated aliphatic acids are probably due to the higher reactivity of chloroacetic acid in comparison to the α-chloropropionic and β acids, despite the relatively higher basicity of benzimidazolin-2-one* (pKa = 10.85 [8]) in comparison to benzoazolin-2-one (pKa = 9.34 [9]) and benzoxazoline-2-thione (pKa = 6.70 [9]) (products of N-carboxyalkylation with β-bromopropionic and β-chlorobutyric acids are nevertheless obtained with the latter [10]).

N-Carboxyethylbenzimidazolin-2-ones IIIa-f (Table 1) were prepared by cyanoethylation of compounds Ia-f in the conditions in [10] with subsequent hydrolysis of N-mono- and N,N'-di-(β-cyanoethyl) derivatives with concentrated hydrochloric acid. It was previously observed [11] that cyanoethylation of benzimidazolin-2-one only takes place in the presence of trimethylphenylammonium or triethylbenzylammonium hydroxide. 1,3-Dicyanoethylbenzimi-

*We will hypothesize that the basicity of the anions of benzimidazolin-2-ones I1-f is in agreement with the basicity of the corresponding bases.

Institute of Phytochemistry, Academy of Sciences of the Uzbek SSR, Tashkent 700170.
Translated from Khimiya Geterotsiklicheskikh Soedinenni, No. 11, pp. 1517-1520. November, 1985. Original article submitted December 18, 1984.

0009-3122/85/2111-1251$09.50

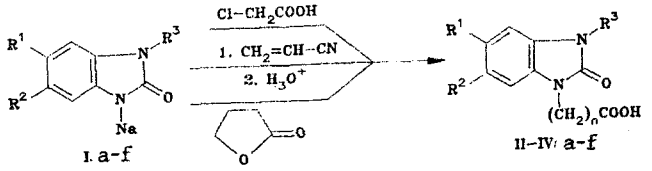
TABLE 1. Characteristics of Synthesized Compounds

Compound	mp, °C (from ethanol)	R_f	M (mass spectrometry)	PMR spectrum, δ, ppm			Found, %			Empirical formula	Calculated, %			Yield, %
				α-Methylene group	β-Methylene group	γ-Methylene group	C	H	N		C	H	N	
IIb	216—217	0,38	264	4,45,s			54,7	4,3	10,3	$C_{12}H_{12}N_2O_5$	54,5	4,5	10,6	45
IIc	221—222	0,36	284	4,33,s			46,8	3,4	10,1	$C_{11}H_9ClN_2O_5$	46,4	3,2	9,8	85
IId	288—289	0,30	278	4,52,s			55,9	5,2	10,2	$C_{13}H_{14}N_2O_5$	56,1	5,0	10,1	9
IIe	196—198	0,45	232	4,57,s			62,1	5,3	12,4	$C_{12}H_{12}N_2O_3$	62,1	5,2	12,1	55
IIf	161—163	0,41	266	4,35,s			54,3	4,1	10,9	$C_{12}H_{11}ClN_2O_3$	54,3	4,1	10,5	58
IIh	216—218	0,30	226	4,47,s			48,0	3,2	12,8	$C_9H_7ClN_2O_3$	47,9	3,1	12,4	100
IIIb	158—159	0,37	292	4,05,t			57,4	5,6	10,0	$C_{14}H_{16}N_2O_5$	57,5	5,5	9,6	40
IIIc	181—183	0,34	312	3,97,t	2,55, t		50,2	4,1	8,8	$C_{13}H_{13}ClN_2O_5$	49,9	4,2	9,0	89
IIId	225—226	0,30	306	4,15,t	2,62, t		59,0	6,1	9,1	$C_{15}H_{18}N_2O_5$	58,8	5,9	9,2	10
IIIe	180—182	0,41	246	4,03,t	2,71, t		63,2	5,8	11,6	$C_{13}H_{14}N_2O_3$	63,4	5,7	11,4	51
IIIf	163—164	0,38	280	3,90,t	2,57, t		56,0	4,6	9,9	$C_{13}H_{13}ClN_2O_3$	55,8	4,7	10,0	12
IIIg	231—233	0,33	206	4,01,t	2,60, t		58,4	5,1	13,3	$C_{10}H_{10}N_2O_3$	58,3	4,9	13,6	100
IIIh	223—225	0,32	240	4,08,t	2,64, t		50,0	3,8	11,8	$C_{10}H_9ClN_2O_3$	50,1	5,9	11,7	100
IVa	98—99	0,36	306	3,70,t	1,85, m	2,20,t	59,0	5,8	9,6	$C_{15}H_{18}N_2O_5$	58,8	5,9	9,2	20
IVb	161—162	0,41	320	3,72,t	1,83, m	2,24,t	61,5	6,3	9,0	$C_{16}H_{20}N_2O_5$	61,3	6,3	8,8	19
IVc	76—77	0,37	340	3,81,t	1,93, m	2,30,t	53,0	5,1	8,0	$C_{15}H_{17}ClN_2O_5$	52,9	5,0	8,2	64
IVd	177—178	0,39	334	3,74,t	1,87, m	2,23,t	61,1	6,7	8,6	$C_{17}H_{22}N_2O_5$	61,1	6,6	8,4	8
IVe	147—149	0,42	260	3,78,t	1,85, m	2,18,t	64,7	6,0	10,9	$C_{14}H_{16}N_2O_5$	64,6	6,1	10,7	29
IVf	200—201	0,43	294	3,69,t	1,82, m	2,21,t	57,2	5,2	9,7	$C_{14}H_{15}ClN_2O_5$	57,2	5,1	9,5	34
IVg	175—176	0,36	220	3,73,t	1,88, m	2,27,t	60,1	5,6	12,9	$C_{11}H_{12}N_2O_3$	60,0	5,5	12,7	100
IVh	182—183	0,31	254	3,79,t	1,93, m	2,31,t	51,8	4,3	11,1	$C_{11}H_{11}ClN_2O_3$	52,1	4,3	11,0	100

dazolin-2-one, which is hydrolyzed into 1,3-dicarboxyethylbenzimidazolin-2-one IIIa, was obtained in this way.

The corresponding 1(3)-mono- and 1,3-dicarboxypropylbenzimidazolin-2-ones (IVa-f) were prepared by alkylation of the sodium salts of benzimidazolin-2-ones Ia-f with γ-butyrolactone in dry DMF with a ratio of compounds Ia-f—γ-butyrolactone of 1:2.2.

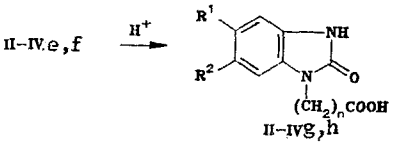
The formation of 1(3)-mono- and 1,3-dicarboxylalkylbenzimidazolin-2-ones IIa-f to IVa-f takes place according to the scheme



I a-f II-IV a-f

Ia,e R^1=H; b,d R^1=CH_3; c,f R^1=Cl; a–c,e,f R^2=H; d R^2=CH_3; a–d R^3=Na; e,f R^3=$-C(CH_3)=CH_2$; II—IV a–d R^3=$(CH_2)_nCOOH$; e,f R^3=$C(CH_3)=CH_2$; II n=1, III n=2, IV n=3

Cleavage of the isopropenyl group takes place in the hydrochloric acid hydrolysis of compounds IIe, f—IVe, f, and the corresponding 1- and 3-carboxylalkylbenzimidazolin-2-ones IIg,h—IVg,h are formed:



II—IV g R^1=H; h R^1=Cl; g,h R^2=H

The structure of compounds IIa-h—IVa-h is demonstrated by the findings of elementary analysis, IR and PMR spectroscopy, and mass spectrometry. The IR spectra of compounds IIa-h—IVa-h contain bands $\nu_{C=O}$ of the carboxyl group (1735-1720 cm^{-1}) and the imidazolinone ring (1690-1680 cm^{-1}) [12]. In the PMR spectra of compounds IIa-h—IVa-h, the protons of the α-, β-, and γ-methylene groups are manifested by the corresponding signals (Table 1).

The study of the pesticide activity of the synthesized compounds showed that the fungicidal activity (for example, against *Verticillium dahliae* Kleb.) of compounds IIa-f and IVa-f is on the whole greater than the activity of compounds IIIa-f. At the same time, the activity of compound IVa is higher than the activity of compound IIa, which is apparently due to an increase in the lipophilic character of the first compound. A similar dependence is also observed for the inhibiting action of the compounds on wheat coleoptiles. We thus experimentally confirmed that N-carboxylalkylbenzimidazolin-2-ones IIa-f and IVa-f with an uneven number of methylene groups are more active than compounds IIa-f with an even number of these groups; this is in agreement with the well-known mechanism of β-oxidation [5] which accounts for the biological activity of some compounds.

EXPERIMENTAL

The mass spectra were made on a MX-1303 spectrometer with an ionizing voltage of 30 eV and at a temperature of 150-210°C with direct introduction of the sample in the ion source; the IR spectra were made on a UR-20 spectrometer (KBr pellets), and the PMR spectra were made on a Joel-C-60H 4/60 instrument in deuterated methanol (HMDS internal standard). TLC was conducted on Silufol UV-254 plates in the propanol—ammonia—ethyl acetate system, 1:3:6; the developer was a 1% solution of $KMnO_4$ in a 4% solution of sulfuric acid.

The characteristics of compounds II-IV are reported in Table 1.

1,3-Dicarboxymethylbenzimidazolin-2-one (IIa). Here 3.8 g (0.04 mole) of chloroacetic acid dissolved in 50 ml of water with 3.5 g $NaHCO_3$ was added to a solution of disoldium salt Ia prepared from 2.68 g (0.02 mole) of benzimidazolin-2-one and 1.6 g (0.04 mole) of sodium hydroxide in 50 ml of water, and the solution was heated for 4 h at 90-95°C. After 15 h, the precipitated sediment of unreacted benzimidazolin-2-one was filtered off, and the filtrate was acidified with a 4 N solution of hydrochlorid acid. Product IIa gradually precipitated from the acid solution. An additional amount of compound IIa was obtained on concentration of the acid solution. Yield of 3.85 g (77%), mp 280-282°C (from ethanol) (according to the data in [6], mp of 282-283°C), R_f 0.40.

Compounds IIb-f were prepared in the same way.

1,3-Dicarboxyethylbenzimidazolin-2-one (IIIa). Over 10-15 min, 4.24 g (0.08 mole) of acrylnotrile (containing 0.01% hydroquinone) was added by drops at 80°C to a solution of the potassium salt of benzimidazolin-2-one prepared from 2.68 g (0.02 mole) of benzimidazolin-2-one and 2.4 g (0.04 mole) of potassium hydroxide in 50 ml of water. The reaction mixture was held at this temperature for 4 h and was acidified with hydrochloric acid after cooling. Then 4.4 g of compound IIIa (80%) were obtained, mp of 187-189°C (from ethanol) (according to the data in [11], mp of 188-189.5°C), R_f 0.31.

Compounds IIIb-f were prepared similarly.

Benzimidazolin-2-one Disodium Salt (Ia). Here 4.6 g (0.2 mole) of metallic sodium was added in portions to 80 ml of absolute ethanol. While stirring, 13.4 g (0.01 mole) of benzimidazolin-2-one was added over 20 min and the ethanol was distilled off. Then 17.8 g of benzimidazolin-2-one disodium salt Ia were obtained with a quantitative yield.

Mono- and disodium salts Ib-f were prepared in the same way.

1,3-Dicarboxypropylbenzimidazolin-2-one (IVa). A mixture of 8.9 g (0.05 mole) of dry, finely ground disodium salt Ia, 10 ml (0.11 mole) of freshly distilled γ-butyrolactone, and 20 ml of dry DMF were heated for 2 h at 150-160°C while stirring and left overnight. The excess DMF was distilled off in an oil bath at 150°C. The solid sediment was hydrolyzed with 50 ml of a 4 N solution of hydrochloric acid. After cooling, compound IVa was separated. When the filtrate was boiled, an additional amount of product IVa was obtained. The yield of compound IVa was 3.0 g (20%), mp 98-99°C.

Compounds IVb-f were prepared in the same way.

1(3)-Carboxymethylbenzimidazolin-2-one (IIg). A mixture of 2.32 g (0.01 mole) of compound IIe and 25 ml of a 4 N solution of HCl was heated for 6 h in a boiling water bath. After cooling, 1.92 g of compound IIg, mp 237-239°C (from ethanol) (according to the data in [7], mp of 237-240°C), R_f 0.31, was obtained with a quantitative yield.

1- and 3-carboxylalkylbenzimidazolin-2-ones (IIh, IIIg, h, IVg, h) were prepared in the same way.

LITERATURE CITED

1. Ch. Sh. Kadyrov, in: Plant Growth Regulators and Herbicides [in Russian], Fan. Tashkent (1978), p. 65.
2. Ch. Sh. Kadyrov, N. D. Livshits, S. A. Khasanov, A. A. Atakuziev, A. V. Gordeeva, and M. Akbarova, in: Fungicides [in Russian], Fan, Tashkent (1980), p. 5.
3. S. Inoue. N. Yamasita, and T. Uematsu, Japanese Patent Application 54-132232; Ref. Zh. Khim., 20ö303P (1980).
4. N. N. Mel'nikov and Yu. A. Baskakov, Chemistry of Herbicides and Plant Growth Regulators [in Russian], Goskhimizdat, Moscow (1962), p. 606.
5. M. S. Smith, R. L. Wein, and F. Sightman, Ann. Appl. Biol., 295 (1952).
6. L. Sawlewicz and W. Kuraszkiewicz. Acat Pol. Pharm., No. 6, 413 (1963).
7. J. Davoll and D. H. Laney, J. Chem. Soc., 314 (1960).
8. Ch. Sh. Kadyrov, A. T. Ayupova, A. A. Umarov, N. P. Loi, and G. A. Nezhinskaya, Fiziol. Rast., 21, 1276 (1974).
9. N. A. Aliev, in: Fungicides [in Russian], Fan. Tashkent (1980), p. 82.
10. N. A. Aliev, R. G. Aflyatunova, and K. Giyasov, in: Fungicides [in Russian], Fan, Tashkent (1980), p. 46.
11. A. M. Efros. Zh. Obshch. Khim., 28, 617 (1958).
12. L. A. Kazitsyna and N. B. Kupletskaya, Use of UV, IR, NMR, and Mass Spectroscopy in Organic Chemistry [in Russian], Izd. MGU, Moscow (1979), p. 211.
13. G. Becker, Introduction to the Electronic Theory of Organic Reactions [Russian translation], Mir, Moscow (1977), pp. 169, 171, 317.