Compounds IIb-d were similarly obtained. An intense absorption band at 1125 cm^{-1} (C–O–C) appeared in the IR spectra of alkoxy derivatives IIa-d. Thioamide bands were found at 1235 and 1505 cm^{-1}.

1-(α-Phenoxyethyl)benzimidazole-2-thione (IIe). A 1.88-g (0.02 mole) sample of phenol and 1.76 g (0.01 mole) of vinyl thione I were added at room temperature in the course of 5 min to 20 ml of benzene saturated with HCl, and the mixture was refluxed for 3 h. The benzene was removed by vacuum distillation, and the solid residue was recrystallized from hot benzene to give 1.08 g (40%) of white crystalline IIe.

2-Methylthiobenzimidazole (IVa). A stream of dry hydrogen chloride was passed for 5-10 min at room temperature into 10 ml of methanol, 1.5 g (0.01 mole) of benzimidazole-2-thione (III) was added, and the mixture was refluxed for 2 h. The excess alcohol was removed *in vacuo*, and the residue was dissolved in 10 ml of water. The solution was made alkaline to pH 8 with concentrated KOH solution, and the resulting white precipitate was removed by filtration, washed with water, and dried to give 1.56 g (95%) of IVa with mp 205-206°C (mp 201°C [4]). IR spectrum: 1370 (CH_3); 1450-1620 (ring C=C, C=N); 1600, 3430 (NH); 3100 cm^{-1} (associated NH). The PMR spectrum contained a singlet of methyl protons at 2.71 ppm and a multiplet of aromatic protons at 7.30 ppm.

Compounds IVb-d were similarly obtained.

LITERATURE CITED

1. N. D. Abramova, G. G. Skvortsova, B. V. Trzhtsinskaya, and M. V. Sigalov, Khim. Geterotsikl. Soedin., No. 12, 1674 (1975).
2. M. L. Martin, F. Lefevre, D. Lapeyre, and G. Martin, J. Org. Magn. Reson., 1, 19 (1969).
3. G. G. Skvortsova, E. S. Domnina, N. P. Glaskova, N. N. Chipanina, and N. I. Shergina, Zh. Obshch. Khim., 41, 623 (1971).
4. K. Futaki, J. Pharm. Soc. Japan, 74, 1365 (1954); Chem. Abstr., 49, 15876 (1955).

FRIEDEL–CRAFTS ACYLATION OF BENZIMIDAZOLIN-2-ONES WITH ALIPHATIC ACID CHLORIDES

Ch. Sh. Kadyrov and S. S. Khalikov

UDC 547.785.5:542.951:543.51'422.25'4

The acylation of benzimidazolin-2-one and its 5,6-disubstituted derivatives with aliphatic acid chlorides in the presence of anhydrous aluminum chloride was studied. The corresponding 5(6)-acyl-, 5-R-6-acyl-, and 5,6-dimethyl-4-acylbenzimidazolin-2-ones, the structures of which were confirmed by the results of elementary analysis and IR, PMR, and mass spectroscopy, were obtained. The yields of the acylation products depend on the electronic effects of the substituents in the benzene ring of the benzimidazolin-2-one and on steric factors.

Many benzimidazole derivatives are highly effective pesticides [1]. The purposeful synthesis of new benzimidazolin-2-one derivatives — analogs of compounds with antibiotic activity [2] — therefore seems promising. In the present research we studied the acylation of benzimidazolin-2-one (I) and its 5-methyl, 5-chloro, 5,6-dimethyl, and 5-(β-carboxypropyl) derivatives (II-V) with aliphatic carboxylic acid chlorides in the presence of anhydrous aluminum chloride in order to ascertain the effect of substituents in the benzene ring of benzimidazolin-2-one, the reactivities of the acyl chlorides themselves with respect to benzimidazolin-2-ones, and steric factors in the 5-R^1-6-R^2-benzimidazolin-2-one series on the yields of the acylation products.

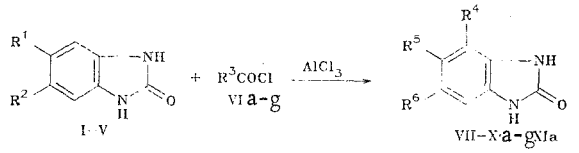
Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 808-811, June, 1984. Original article submitted May 12, 1983.

0009-3122/84/2006-0658$08.50

The available literature data [3-5] on the acylation of benzimidazolin-2-one with several aliphatic acyl chlorides do not provide an answer to the questions posed above. Data on the biological activity of C-acylbenzimidazolin-2-ones are also lacking.

The acylation was carried out at a benzimidazolin-2-one (I-V)—acyl chloride—$AlCl_3$ ratio of 1:2:4 by heating at 90-100°C in tetrachloroethylene for 1 h.



I $R^1=R^2=H$; II $R^1=CH_3$, $R^2=H$; III $R^1=Cl$, $R^2=H$; IV $R^1=R^2=CH_3$; V $R^1=$ $=-CH(CH_3)CH_2COOH$, $R^2=H$; VI a $R^3=CH_3$, b $R^3=CH_2Cl$, c $R^3=C_2H_5$, d $R^3=n\text{-}C_3H_7$, e $R_3=i\text{-}C_3H_7$, f $R^3=n\text{-}C_4H_9$, g $R^3=i\text{-}C_4H_9$; VIIa—g $R^4=R^6=H$, $R^5=COR^3$; VIIIa—g $R^4=H$, $R^5=CH_3$, $R^6=COR^3$; IXa—g $R^4=H$, $R^5=Cl$, $R^6=COR^3$; Xa—g $R^5=R^6=CH_3$, $R^4=COR^3$; XIa $R^4=H$, $R^6=COCH_3$, $R^5=-CH(CH_3)CH_2COOH$

Under these conditions we were able to increase the yields of VIIa,d,f, which were previously synthesized in [3-5], and were also able to obtain new benzimidazolin-2-ones in high yields.

The structures of VII—Xa-g and XIa were proved by the results of elementary analysis and IR, PMR, and mass spectroscopy.

The IR spectra of VIIa-g contain absorption bands at 805-825 and 870-885 cm^{-1}, which are characteristic for 1,2,4-substitution of the benzene ring, whereas an absorption band at 855-870 cm^{-1}, which corresponds to 1,2,4,5-substitution, is characteristic for VIII, IXa-g, and XIa, and an absorption band of pentasubstitution at 870 cm^{-1} is characteristic for Xa-g. A C=O absorption band of a benzimidazolone ring at 1715-1725 cm^{-1} and a C=O absorption band of an acyl residue at 1680-1700 cm^{-1} [6] are observed in the IR spectra of VII—Xa-g and XIa.

The mass spectra of VII—Xa-g and XIa are characterized by the presence of the corresponding molecular-ion peaks (M^+) (Table 1). Thus a molecular-ion peak with m/z 176 (66%) and peaks of fragments with m/z 161 (100%, $M^+ - CH_3$) and 133 (24%, $M^+ - COCH_3$) are observed for VIIa. The mass spectrum of VIIIb is characterized by a molecular-ion peak with m/z 224 (53%) and by peaks of fragments with m/z 175 (100%, $M^+ - CH_2Cl$) and 147 (35%, $M^+ - COCH_2Cl$).

The PMR spectra of VIId and VIIe were studied to confirm the structures of the acyl residues. The aromatic protons for both compounds show up at 7.1-7.9 ppm. The PMR spectrum of VIId is characterized by the presence of signals of protons of an α-methylene group (with respect to the C=O bond of the acyl residue) in the form of a triplet at 2.6-2.9 ppm, protons of a β-methylene group in the form of a sextet at 1.25-1.75 ppm, and methyl protons in the form of a triplet at strong field at 0.5-0.8 ppm.

The PMR spectrum of VIIe contains a signal of a methylidyne proton in the form of a multiplet at 1.6-2.1 ppm and signals of protons of two methyl groups in the form of a six-proton doublet at 0.6-0.75 ppm.

In contrast to syntheses with aromatic compounds [7], a large excess of $AlCl_3$ is necessary in the acylation of benzimidazolin-2-ones in view of bonding of the benzimidazolin-2-one with a molecule of $AlCl_3$, probably at the oxygen atom.

The higher yields of products of acylation with chloroacetyl chloride as compared with acetyl chloride (compare the yields of VIIa,b, VIIIa,b, IXa,b, and Xa,b in Table 1) are in agreement with the literature data [8].

As in other electrophilic substitution reactions (carboxyalkylation [9]), 5-chlorobenzimidazolin-2-one (III) is less active in acylation reactions because of the negative induction effect of chlorine and possible bonding of a molecule of $AlCl_3$ at the chlorine atom due to the basicity of the latter.

A steric effect is manifested appreciably in the reactions that we investigated. Thus the corresponding acylation products Xa-g were obtained in low yields (10-29%) (Table 1) in the acylation of 5,6-dimethylbenzimidazolin-2-one (IV). Steric hindrance is also manifested in the acylation of 5-substituted benzimidazolin-2-ones (II-IV). Thus reaction products VIIIg and IXg were obtained in lower yields in the acylation of 5-methylbenzimidazolin-2-one (II)

TABLE 1. Characteristics of the Benzimidazolin-2-one Derivatives

Compound	mp, °C (from 50% aqueous ethanol)	M^+ (by mass spectrometry)	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
VIIb	276—278	210	51,1	3,4	13,4	$C_9H_7ClN_2O_2$	51,4	3,3	13,2	98
VIIc	247—249	190	63,2	5,2	14,6	$C_{10}H_{10}N_2O_2$	63,2	5,3	14,7	95
VIIe	245—247	204	64,7	5,9	13,7	$C_{11}H_{12}N_2O_2$	64,7	5,9	13,7	96
VIIIa	250—252	190	63,2	5,3	14,7	$C_{10}H_{10}N_2O_2$	63,2	5,3	14,7	96
VIIIb	260—262	224	53,3	4,0	12,7	$C_{10}H_9ClN_2O_2$	53,5	4,0	12,4	98
VIIIc	235—237	204	64,7	5,9	13,8	$C_{11}H_{12}N_2O_2$	64,7	5,9	13,7	98
VIIId	212—214	218	66,1	6,4	12,9	$C_{12}H_{14}N_2O_2$	66,1	6,4	12,8	89
VIIIe	238—240	218	66,1	6,5	12,7	$C_{12}H_{14}N_2O_2$	66,1	6,4	12,8	91
VIIIf	231—233	232	67,3	7,0	12,0	$C_{13}H_{16}N_2O_2$	67,2	6,9	12,1	98
VIIIg	202—204	232	67,3	6,9	12,1	$C_{13}H_{16}N_2O_2$	67,2	6,9	12,1	82
IXa	257—259	210	51,3	3,4	13,4	$C_9H_7ClN_2O_2$	51,4	3,3	13,3	79
IXb	253—255	244	44,0	2,5	11,5	$C_9H_6Cl_2N_2O_2$	43,9	2,4	11,4	89
IXc	246—248	224	53,6	4,1	12,6	$C_{10}H_9ClN_2O_2$	53,5	4,0	12,5	90
IXd	250—252	238	55,4	4,8	11,8	$C_{11}H_{11}ClN_2O_2$	55,3	4,6	11,7	80
IXe	285—287	238	55,2	4,6	11,8	$C_{11}H_{11}ClN_2O_2$	55,3	4,6	11,8	78
IXf	248—250	252	57,1	5,2	11,0	$C_{12}H_{13}ClN_2O_2$	57,0	5,2	11,1	88
IXg	215—217	252	57,2	5,2	11,4	$C_{12}H_{13}ClN_2O_2$	57,0	5,2	11,1	67
Xa	217—219	204	64,6	5,7	13,9	$C_{11}H_{12}N_2O_2$	64,7	5,9	13,7	25
Xb	281—283	238	55,2	4,7	11,5	$C_{11}H_{11}ClN_2O_2$	55,1	4,6	11,7	29
Xc	288—290	218	66,1	6,5	12,9	$C_{12}H_{14}N_2O_2$	66,1	6,4	12,8	28
Xd	188—190	232	67,1	7,0	12,2	$C_{13}H_{16}N_2O_2$	67,2	6,9	12,1	16
Xe	222—224	232	67,1	6,8	12,3	$C_{13}H_{16}N_2O_2$	67,2	6,9	12,1	12
Xf	186—187	246	68,4	7,4	11,5	$C_{14}H_{18}N_2O_2$	68,3	7,3	11,4	30
Xg	180—182	246	68,3	7,2	11,3	$C_{14}H_{18}N_2O_2$	68,3	7,3	11,4	10
XIa	340—342	262	50,3	5,4	10,8	$C_{13}H_{14}N_2O_4$	50,4	5,3	10,7	52

and 5-chlorobenzimidazolin-2-one (III) with VIg with an iso structure than in the case of acylation with acid chlorides with a normal structure (to give VIIIf and IXf). 5-(β-Carboxypropyl)-6-acetylbenzimidazolin-2-one (XIa) was obtained in low yield (52%) (Table 1) in the acylation of 5-(β-carboxypropyl)benzimidazolin-2-one (V) with acetyl chloride.

It is apparent from the data obtained that the acylation of benzimidazolin-2-one and 5-substituted derivatives II and III with aliphatic acid chlorides occurs readily (in the presence of anhydrous aluminum chloride), and this in turn indicates the high reactivities of acyl chlorides with respect to benzimidazolin-2-ones. We have established that the yields of the acylation products depend on the electronic effects of the substituents in the benzene ring of the benzimidazolin-2-one and steric factors. 5(6)-Acyl derivatives VIIa-g are obtained in the acylation of benzimidazolin-2-one (I); this is in agreement with the literature data on the reactivities of the 4, 5, 6, and 7 positions in the I molecule [10]. Acylation of 5-substituted benzimidazolin-2-ones II, III, and V, however, leads to the formation of the corresponding 6-acyl derivatives VIIa-g, IXa-g, and XIa. In the case of 5,6-dimethylbenzimidazolin-2-one (IV) the acyl group is incorporated in the 4(7) position to give the corresponding Xa-g.

It is known that C-aroylbenzimidazolin-2-ones are biotin antagonists and are capable of inhibiting the growth of malignant tumors [2]. A study of the herbicidal activity of the compounds that we synthesized was carried out on the seedlings and rootlets of four plants (cucumbers, radishes, cabbage, and wheat). All of the C-acylbenzimidazolin-2-ones displayed weak herbicidal activity with respect to cucumbers. Whereas a decrease in the herbicidal activity with respect to radishes was observed with an increase in the length of the acyl residue in the 5-chloro-6-acylbenzimidazolin-2-one series (IXa-e), the introduction of a chloroacetyl group (IXb) in place of an acetyl group into the benzene ring (IXa) increased the herbicidal effect with respect to cabbage and wheat. The introduction of an electron-donor substituent (CH_3) (VIIIb) and an electron-acceptor substituent (Cl) (IXb) into the position adjacent to $COCH_2Cl$ increased the herbicidal activity of the compounds with respect to radishes and cabbage. Branching of the acyl residue (IXe and IXg) promotes an increase in the herbicidal effect on radishes and a decrease in the herbicidal effect on cabbage and wheat.

EXPERIMENTAL

The mass spectra were recorded with an MKh-1303 spectrometer at an ionization energy of 30 eV and an input-system temperature of 150-210°C with direct introduction of the samples into the ion source. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions in trifluoroacetic acid were obtained with a Jeol C-60HL/60 spectrometer with hexamethyldisiloxane as the internal standard.

5-Acetylbenzimidazolin-2-one (VIIa). A 5.34-g (0.04 mole) sample of anhydrous $AlCl_3$ was added in portions with constant stirring and cooling with water to a suspension of 1.34 g (0.01 mole) of I in 50 ml of tetrachloroethylene, after which a solution of 1.57 g (0.02 mole) of acetyl chloride in 10 ml of tetrachloroethylene was added dropwise in the course of 5-10 min, and the mixture was heated at 90-100°C for 1 h, during which the color changed successively from white to crimson to black. The congealed mass was hydrolyzed with a mixture of 50 g of ice and 25 ml of 4 N HCl, and the tetrachloroethylene was removed by steam distillation. The white VIIIa that precipitated in the acidic aqueous solution was recrystallized from 50% aqueous ethanol to give 1.62 g (92%) of VIIa with mp 280-282°C (mp 280-285°C [4]). Found: C 61.2; H 4.6; N 16.0%. $C_9H_8N_2O_2$. Calculated: C 61.4; H 4.5; N 15.9%.

Compounds VIIb-g, VIII–Xa-g, and XIa were similarly obtained.

5-Butyrylbenzimidazolin-2-one (VIId). This compound was obtained in 83% yield and had mp 261-263°C (50% aqueous ethanol) (mp 261-263°C [4]). Found: C 64.8; H 5.9; N 13.8%. $C_{11}H_{12}N_2O_2$. Calculated: C 64.7; H 5.9; N 13.7%.

5-Valerylbenzimidazolin-2-one (VIIf). This compound was obtained in 92% yield and had mp 235-237°C (50% aqueous ethanol) (mp 269-271°C [5]). Found: C 66.1; H 6.5; N 12.8%. $C_{12}H_{14}N_2O_2$. Calculated: C 66.1; H 6.4; N 12.8%.

5-Isovalerylbenzimidazolin-2-one (VIIg). This compound was obtained in 98% yield and had mp 251-253°C (50% aqueous ethanol) (mp 268-270°C [5]). Found: C 66.0; H 6.5; N 12.8%. $C_{12}H_{14}N_2O_2$. Calculated: C 66.1; H 6.4; N 12.8%.

LITERATURE CITED

1. N. N. Mel'nikov, The Chemistry and Technology of Pesticides [in Russian], Khimiya, Moscow (1974), p. 636.
2. Yu. A. Rozin, E. P. Darienko, and Z. V. Pushkareva, Khim. Geterostikl. Soedin., No. 4, 698 (1968).
3. A. V. El'tsov and N. M. Ginzburg, Zh. Obshch. Khim., 34, 1624 (1964).
4. J. R. Vaughan and J. J. Blodinger, J. Am. Chem. Soc., 77, 5757 (1955).
5. R. L. Clark and A. A. Pesolano, J. Am. Chem. Soc., 80, 1657 (1958).
6. L. A. Kazitsyna and N. B. Kuplet-skaya, Application of UV, IR, NMR, and Mass Spectroscopy in Organic Chemistry [in Russian], Izd. Moskovsk. Gosudarstv. Univ., Moscow (1979), p. 211.
7. Ch. Sh. Kadyrov, Uzb. Khim. Zh., No. 2, 52 (964).
8. P. N. Gore and J. A. Hoskins, Chem. Commun., No. 22, 835 (1966).
9. Ch. Sh. Kadyrov, M. N. Kosyakovskaya, and M. R. Yagudaev, Uzb. Khim. Zh., No. 3, 39 (1968).
10. L. S. Éfros and A. V. El'tsov, Zh. Obshch. Khim., 27, 127 (1957).