ACYLATION OF BENZIMIDAZOLONE AND ITS DERIVATIVES WITH ACID ANHYDRIDES AND ACID CHLORIDES

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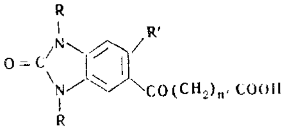
N,N'-Diacetyl derivatives of benzimidazolones were obtained by the acylation of benzimidazoline and its 5-methyl, 5-chloro, and 5-nitro derivatives with acetic, propionic, and butyric anhydrides and also with monochloro- and monobromoacetyl chlorides.

Benzimidazolone derivatives stimulate the growth and blossoming of plants and increase the yield, fructification, and resistance of plants to wilt [1]. In order to find new chemotherapeutic agents to counter cotton plant wilt, we studied the acylation of benzimidazolone and its derivatives with acid anhydrides and chlorides.

The C-acylation of benzimidazolone with succinic and glutaric anhydrides in the presence of a fivefold excess of anhydrous aluminum chloride to give 9 and 5% yields of the products, respectively, has been described [2]. We introduced changes into this method and extended it to 5-methyl- (III) and N,N'-dimethyl-

TABLE 1. 5(6)-(3-Carboxy-1-propionyl)- and 5(6)-(4-Carboxy-1-butyryl)benzimidazolones



Compound	R	R'	Mp, °C	Empirical formula	λ_{max}, nm (lg ε)	Methyl ester, mp, °C	Yield, %
IV*	H	H	293—294	$C_{11}H_{10}N_2O_4$	219 (4,282), 285 (4,222), 282 (3,927), 309 (3,861)	246—247	50 (3,5) †
V	CH_3	H	243—244	$C_{13}H_{14}N_2O_4$	226 (4,423), 239 (4,367), 286 (4,046), 312 (4,046)	188—189	40 (3,5)
VI	H	CH_3	262—263	$C_{12}H_{12}N_2O_4$	222 (4,290), 236 (3,926), 278 (3,845), 310 (3,810)	213—214	50 (3,6)
VII*	H	H	261—262	$C_{12}H_{12}N_2O_4$	219 (4,286), 236 (4,234), 288 (3,887), 311 (3,927)	210—211	32 (3,5)
VIII	CH_3	H.	217—218	$C_{14}H_{16}N_2O_4$	227 (4,44), 238 (4,41), 288 (4,01), 312 (4,03)	165—166	34 (3,5)
IX	H	CH_3	220—221	$C_{13}H_{14}N_2O_4$	224 (4,38), 237 (4,39), 282 (3,91), 313 (4,02)	171—172	29,5 (3,5)

* These compounds were first obtained in [2].

† The number of moles of $AlCl_3$ per mole of reagents is indicated in parentheses.

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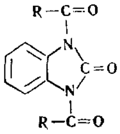
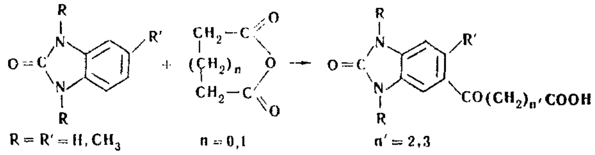
TABLE 2. N,N'-Diacylbenzimidazolones



Starting reagents	Heating time, h	Reaction products	Mp, °C	λ_{max}, nm (lg ε)	Yield, %
Benzimidazolone : acetic anhydride	5	N,N'-Diacetylbenzimidazolone	139	238 (3,97), 281 (3,12)	92
Benzimidazolone : propionic anhydride	5	N,N'-Dipropionylbenzimidazolone	162	246 (4,01), 283 (3,12)	94
Benzimidazolone : butyric anhydride	5	N,N'-Dibutyrylbenzimidazolone	126	238 (3,95), 281 (2,99)	92
5-Methylbenzimidazolone : acetic anhydride	3	5-Methyl-N,N'-diacetylbenzimidazolone	169	241 (3,96), 286 (3,14)	66
5-Methylbenzimidazolone : propionic anhydride	3,5	5-Methyl-N,N'-dipropionylbenzimidazolone	158	241 (4,04), 286 (3,26)	97
5-Methylbenzimidazolone : butyric anhydride	7	5-Methyl-N,N'-dibutyrylbenzimidazolone	55	244 (3,86), 286 (3,06)	76
5-Chlorobenzimidazolone : acetic anhydride	12	5-Chloro-N,N'-diacetylbenzimidazolone	165	238 (3,94), 281 (3,00)	43
5-Chlorobenzimidazolone : propionic anhydride	7	5-Chloro-N,N'-dipropionylbenzimidazolone	145	245 (3,98), 283 (3,32)	90
5-Chlorobenzimidazolone : butyric anhydride	6	5-Chloro-N,N'-dibutyrylbenzimidazolone	65	247 (4,01), 283 (3,32)	43
5-Nitrobenzimidazolone : acetic anhydride	7	5-Nitro-N,N'-diacetylbenzimidazolone	119	228 (4,17), 298 (3,86)	67
5-Nitrobenzimidazolone : propionic anhydride	7	5-Nitro-N,N'-dipropionylbenzimidazolone	157	225 (4,12), 297 (3,50)	51
5-Nitrobenzimidazolone : butyric anhydride	7	5-Nitro-N,N'-dibutyrylbenzimidazolone	142	230 (4,12), 300 (3,82)	37
Benzimidazolone : monochloroacetyl chloride	2	N,N'-Dibromoacetylbenzimidazolone	175	228 (4,18)	50
5-Chlorobenzimidazolone : monochloroacetylchloride	2	5-Chloro-N,N'-dichloroacetylbenzimidazolone	152	226 (4,20), 292 (3,74)	66
5-Nitrobenzimidazolone: monochloroacetyl chloride	2	5-Nitro-N,N'-dichloroacetylbenzimidazolone	207	224 (4,15), 262 (4,07) 340 (3,89)	33
Benzimidazolone : monobromoacetyl chloride	2	N,N'-Dibromoacetylbenzimidazolone	153	228 (4,34)	—
5-Chlorobenzimidazolone : butyric anhydride : water	2	5-Chloro-N-butyrylbenzimidazolone	230	228 (4,26), 260 (3,74)	90
Benzimidazolone :acetyl chloride : dimethylaniline	0,5	N-Acetylbenzimidazolone	205	222 (4,29), 255 (3,74)	—
5-Chlorobenzimidazolone : monobromoacetyl chloride	2	5-Chloro-N,N'-dibromoacetylbenzimidazolone	160	224 (4,33), 292 (4,10)	86
5-Nitrobenzimidazolone: monobromoacetyl chloride	2	5-Nitro-N,N'-dibromoacetylbenzimidazolone	170	224 (4,5), 253 (4,43), 235 (4,27)	—

benzimidazolones (II). The reaction was carried out in tetrachloroethane or without a solvent, and 3.5 moles of anhydrous aluminum chloride were used per mole of starting reagent. The product yields were 30-50%.



The acylation of benzimidazolone (I) and 5-methylbenzimidazolone (III) proceeds to give identical yields, while the product yield decreases in the case of the N,N'-dimethyl derivative (II), which is possibly associated with its higher basicity (pK_a 11.46) as compared with the basicity of benzimidazolone (pK_a 11.56) [3]. In accordance with the literature data [4, 5] for the electrophilic substitution reactions of benzimidazolones, the acylation of I-III with succinic and glutaric anhydrides proceeds at the 5(6) position of the benzene ring. Absorption bands of the CO groups of the imidazolone ring and of the acyl and carboxyl groups (1660-1670, 1690-1705, and 1720-1750 cm^{-1}) are observed in the IR spectra of IV-IX. The absorption bands at 815-820 and 865-875 cm^{-1} correspond to a 1,2,3-substituted benzene ring, while the absorption band at 880 cm^{-1} corresponds to a 1,2,4,5-substituted benzene ring. Four maxima are noted in the UV spectra of IV-IX: two of the maxima, as in I-III, develop due to absorption of the benzimidazolone ring, while the other two develop due to the absorption of the acyl carbonyl group in conjugation with the aromatic ring.

The following signals (δ, ppm) are found in the PMR spectrum of 5-(3-carboxy-1-propionyl)-N,N'-dimethylbenzimidazolone: 2.57 (α-CH_2, I), 3.2 (β-CH_2, I), 3.2 (N$-CH_3$, C), 6.76 (6-CH, D), 7.25 (7-CH, D), 7.23 (4-CH, C).

The imidazole ring of benzimidazolone and its 5-methyl, 5-chloro, and 5-nitro derivatives was acylated with acid anhydrides via the method in [6].

It is apparent from Table 2 that benzimidazolone is acylated most readily and transitions from lower to higher acylating agents do not affect the yield of products. Benzimidazolone and its derivatives are not acylated by halo acid chlorides via the method in [7]. The reaction can be carried out only in the presence of dimethylaniline.

EXPERIMENTAL

The PMR spectra in trifluoroacetic acid were recorded with a JNM 4H-100 spectrometer with an operating frequency of 100 MHz with tetramethylsilane as the standard. The mass spectra were recorded with an MKh-1303 spectrometer with an ionizing voltage of 40 V at 90°. Benzimidazolones I-III were obtained by the method in [4].

5-(3-Carboxy-1-propionyl)benzimidazolone (IV). A 14-g (0.095 mole) sample of anhydrous aluminum chloride was added in small portions to a mixture of 4 g (0.03 mole) of benzimidazolone and 3 g (0.03 mole) of succinic anhydride in 100 ml of tetrachloroethane, and the mixture was heated at 100-120° for 2 h. It was then cooled and poured into a mixture of 20 ml of concentrated HCl and ice. The tetrachloroethane was removed by steam distillation, and the dark-brown powder that precipitated on cooling was separated and dissolved in boiling sodium bicarbonate solution. The solution was treated with charcoal and acidified with concentrated HCl. A portion of the substance was isolated as a powder, while a crystalline product precipitated from the acidic filtrate on standing to give 3.5 g (50%) of IV with mp 293-294° (from acetic acid).

5-(3-Carboxy-1-propionyl)-N,N'-dimethylbenzimidazolone (V). A 3.24-g (0.02 mole) sample of N,N'-dimethylbenzimidazolone and 2 g (0.02 mole) of succinic anhydride were triturated, the mixture was transferred to a flask, and 8.64 g (0.065 mole) of anhydrous aluminum chloride was added. The powdery mixture was stirred and heated at 100-120° for 2 h. It was then cooled and decomposed with 20 ml of concentrated HCl and ice. The solid material was separated and refluxed in sodium bicarbonate solution. The mixture was then treated with charcoal and acidified with concentrated HCl. A portion of the substance was isolated as a powder, while a crystalline product precipitated from the acidic filtrate on standing to give 2.8 g (40%) of V with mp 243-244° (from aqueous acetic acid). Mass spectrum of the methyl ester of V: M^+ with m/e 276, ion peak with m/e 261 ($M-CH_3$), ion peak with m/e 245 ($M-OCH_3$), ion peak with m/e 217 ($M-COOCH_3$), ion peak with m/e 203 ($M-CH_2COOCH_3$), ion peak with m/e 189 ($M-CH_2CH_2COOCH_3$), ion peak with m/e 161 ($M-COCH_2CH_2COOCH_3$). Compounds VI-IX (Table 1) were similarly obtained. The methyl esters (Table 1) were obtained by treatment of IV-IX with diazomethane.

N,N'-Dichloroacetylbenzimidazolone. A total of 5 ml of monochloroacetyl chloride was added with stirring to a mixture of 1.34 g (0.026 mole) of benzimidazolone and 4 ml of dimethylaniline in 20 ml of dry benzene, and the mixture was stirred for 1 h, refluxed for 21 h, and allowed to stand overnight. The product was washed on the filter with water to give a crystalline substance with mp 175° (from ethyl acetate).

N-Acetylbenzimidazolone. A 3.3-g (0.04 mole) sample of acetyl chloride was added slowly with cooling and stirring to a mixture of 1.34 g (0.026 mole) of benzimidazolone and 4 ml of dimethylaniline in 15 ml of dry benzene. The mixture was heated for 30 min, and 30 ml of water was added to give 0.8 g (50%) of a crystalline product with mp 205° (from ethyl acetate).

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