INVESTIGATIONS OF BENZIMIDAZOLE DERIVATIVES

XXV.* SYNTHESIS OF 3-(1'-METHYL-2'-BENZIMIDAZOLYL)ACRYLIC ACID AND ITS DERIVATIVES

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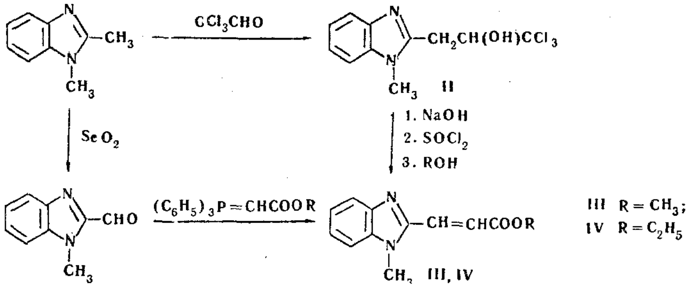
3-(1'-Methyl-2'-benzimidazolyl)acrylic acid was obtained by the reaction of 1,2-dimethylbenzimidazole with chloral and subsequent hydrolysis of the condensation product. The hydrochloride of the chloride of this acid and its esters and amides were synthesized. The methyl and ethyl esters of the acid were synthesized by the Wittig reaction. The IR and UV spectra of the compounds obtained are presented.

Although 2-benzimidazolylacrylic acids have been proposed as the starting compounds for the synthesis of bis(benzimidazolyl)ethylenes [1], which are used for the optical whitening of fabrics, they currently have received little study [1, 2]. We have accomplished the synthesis of 3-(1'-methyl-2'-benzimidazolyl) acrylic acid (I) via two routes. 1,2-Dimethylbenzimidazole, which, as is well known, contains a reactive methyl group in the 2 position, was condensed with chloral, and the 1,1,1-trichloro-3-(1'-methyl-2'-benzimidazolyl)-2-propanol (II) formed was hydrolyzed to I. As in the case of quinaldine [3], the reaction proceeds quite smoothly. Heating I with thionyl chloride converted it to the acid chloride, which was obtained in the form of the hydrochloride; esters (III, IV) and substituted amides (V-VII) (see Table 1) were obtained from the latter via the usual route. Compounds III were also synthesized by the action of diazomethane on I; esterification with methanol in the presence of sulfuric acid did not give satisfactory results.

The other route for the synthesis of I was based on the use of the Wittig reaction, which is apparently the first case of the application of this reaction to the imidazole series.



Compounds III and IV were synthesized by the reaction of 2-formyl-1-methylbenzimidazole [4] with carbomethoxy- and carbethoxymethylenetriphenylphosphoranes; like the acid formed during their saponification with alcoholic alkali, they do not depress the melting points in mixed samples with compounds obtained via the first method. The identical character of the compounds obtained is also confirmed by the results of thin-layer chromatography (aluminum oxide, chloroform) and by their UV spectra. In both cases, strong absorption bands characteristic for the CO (1700 cm^{-1}) and C=C (1665 cm^{-1}) valence vibrations

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*See [9] for Communication XXIV.

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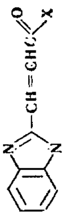
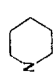
and out-of-plane =CH (970cm^{-1}) vibrations [6] appear in the IR spectra of I obtained from mineral-oil suspensions with a UR-20 spectrophotometer.

These results indicate that the compounds obtained by means of the two methods have the same configuration. They are apparently the trans forms since the formation of trans isomers is generally observed [7, 8] when resonance-stabilized alkylidenephosphoranes (as are the carbalkoxymethylenetriphenylphosphoranes) are used.

TABLE 1



Compound	X	Mp, °C	Crystallization solvent	Empirical formula	Found %			Calculated %			UV spectra (in methanol)		Yield, %
					C	H	N	C	H	N	λ_{max}	lg ε	
III	OCH_3	130	Aqueous dioxane	$C_{12}H_{12}N_2O_2$	66,98	5,87	12,92	66,65	5,72	12,95	261 324	2,55 4,32	86,0
IV	OC_2H_5	102	Aqueous alcohol	$C_{13}H_{14}N_2O_2$	68,1	6,47	12,01	67,81	6,13	12,16	263 329	2,80 4,28	85,0
V	HNC_6H_5	216—217	Alcohol	$C_{17}H_{15}N_3O$	73,52	5,70	15,15	73,62	5,45	15,15	262 336	3,39 4,33	86,6
VI	$N(C_2H_5)_2$	77—78	Water	$C_{15}H_{19}N_3O \cdot 2H_2O$*	61,42	7,69	14,44	61,42	7,90	14,32	262 330	3,62 4,37	90,4
VII		100	Aqueous alcohol	$C_{16}H_{19}N_3O \cdot 2H_2C$†	62,69	7,39	13,70	62,92	7,59	13,76	262 323	3,30 4,06	65,5

*Found %: H_2O 11.96. Calculated %: H_2O 12.27.

†Found %: H_2O 11.47. Calculated %: H_2O 11.79.

EXPERIMENTAL

1,1,1,-Trichloro-3-(1'-methyl-2'-benzimidazolyl)-2-propanol (II). Anhydrous zinc chloride (0.3-0.5 g) was added to a solution of 14.6 g (0.1 mole) of 1,2-dimethylbenzimidazole in 20 ml of dry toluene, and 9.6 ml (0.1 mole) of chloral in 10 ml of toluene was added. The mixture was heated for 3 h with stirring on a water bath at 90-95°. It was then cooled, and the resulting precipitate was filtered and washed with ethanol to give 20 g (68%) of colorless plates with mp 201-202° (from toluene). Found %: C 44.80; H 3.80; N 9.64. $C_{11}H_{11}Cl_3N_2O$. Calculated %: C 45.00; H 3.78; N 9.54.

3-(1'-Methyl-2'-benzimidazolyl)acrylic Acid (I). A mixture of 29.3 g (0.1 mole) of II, 80 ml of ethanol, and 100 ml of 25% sodium hydroxide was heated cautiously until a very vigorous reaction commenced (when necessary, the flask was cooled with ice water). The solution was then refluxed for 2-3 h, the alcohol was removed in vacuo, and 50-60 ml of concentrated hydrochloric acid was added in portions with cooling. The precipitate of the hydrochloride of I was filtered and dissolved in the minimum amount of 10% sodium hydroxide. The free acid [15.8 g (61%)] was isolated by careful acidification with dilute hydrochloric acid. The product was obtained in the form of colorless plates with mp 227-228° (decomp., dioxane with water) that were slightly soluble in water and alcohol and insoluble in benzene. The compound readily decolorizes bromine water and potassium permanganate solution. Found %: C 65.43; H 5.04; N 13.9. $C_{11}H_{10}N_2O_2$. Calculated %: C 65.34; H 4.98; N 13.95. λ_{max} (log ε): 260, 317 nm (3.08, 3.98).

Hydrochloride of the Acid Chloride of I. This was obtained by heating I with a small excess of thionyl chloride for 1 h at 80°. The excess thionyl chloride was removed in vacuo, and the residue was dried at 80°. The product was placed in excess alcohol to obtain the esters of I; the amides were formed by mixing it with 2 moles of amine.

Methyl Ester of I (III). 1-Methyl-2-formylbenzimidazole [0.8 g (5 mmole)] was refluxed for 5 h in 15 ml of benzene with 1.67 g (5 mmole) of carbomethoxymethylenetriphenylphosphorane, and the mixture was cooled and shaken with 10% hydrochloric acid. The hydrochloric acid extract was separated and neutralized with sodium bicarbonate solution, and the precipitated ester was filtered to give 0.75 g (70%) of product.

Compounds III and IV were hydrolyzed to I by refluxing them in an alcoholic solution of potassium hydroxide for 4 h.

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