NEW 2-METHYLBENZIMIDAZOLE DERIVATIVES

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New 2-methylbenzimidazole derivatives with a methyl, ethyl, or phenyl group at position 1, and a hydroxymethyl, aldehyde, or β -carboxyl group at position 5 are synthesized. Imidocyanine dyes with aldehyde and β -carboxyl groups in the heterocyclic portions are obtained, and their main light absorption maxima determined.

2-Methylbenzimidazole derivatives with hydroxymethylene or formyl groups in the benzene ring have so far not been described. Methyl or ethyl esters of 1-alkyl (or phenyl)-2-methylbenzimidazole-5-carboxylic acids have now been reduced with lithium aluminum hydride to good yields of benzimidazole carbinols (I-III).



I $R=HOCH_2$, $R'=CH_3$; II $R=HOCH_2$, $R'=C_2H_5$. III $R=HOCH_2$, $R'=C_6H_5$; IV R=CHO, $R'=CH_3$. V R=CHO, $R'=C_2H_5$; VI R=CHO, $R'=C_6H_5$; VII R=HOOC-CH=CH, $R'=CH_3$; VIII R=HOOC-CH=CH, $R'=C_2H_5$. IX R=HOOC-CH=CH, $R'=C_6H_5$.

Oxidation of these latter with chromic anhydride-acetic acid proceeds similarly to the corresponding oxidation of 2-methylbenzothiazole [1], giving 1-alkyl (or phenyl)-2-methylbenzimidazole-5-aldehydes (IV-VI). The carbinols I-III and aldehydes IV-VI are relatively high-melting, colorless, odorless compounds, giving quaternary salts when heated with alkyl halides. The aldehydes IV-VI readily condense with substances containing an active methylene group, e.g., malonic acid, 3-ethylrhodanine, and consequently are convenient starting materials for synthesis of new 2-methylbenzi-midazole derivatives. The aldehydes IV-VI condense with malonic acid in the presence of α -picoline, giving benzimi-dazoleacrylic acids (VII-IX), while they similarly condense with 3-ethylrhodanine to give benzimidazolylmethylener-hodanine (X-XII).

Cyanine dyes have been synthesized from the new 2-methylbenzimidazole derivatives with a phenyl group at position 1 for the purpose of comparing their optical and photographic properties with those of imidocyanines previously described by the present authors [2].

Dimethylmerocyanines containing the 3-ethylrhodanine grouping (XIII-XIV), and symmetrical imidocarbocyanines (XVI-XVII) have been prepared.



XV R=CHO, R'=CH₃; XVI R=HOOC-CH=CH, R'=C₂H₆.

Introduction of the aldehyde group or, in particular, of the β -carboxyvinyl group into imidocarbocyanines has a favorable effect on their sensitizing properties.

Experimental

<u>1, 2-Dimethyl-5-hydroxymethylbenzimidazole (I)</u>. A solution of 20.4 g (0.1 mole) methyl 1, 2-dimethylbenzimidazole-5-carboxylate [2] in 150 ml tetrahydrofuran was heated to 60°, and added over 50 min, with stirring, to a solution of 4.75 g (0.125 mole) lithium aluminium hydride in 250 ml ether plus 50 ml tetrahydrofuran. Despite the exothermic reaction, the mixture was not cooled. Stirring was continued for a further 50 min after completion of addition, 100 ml water then added, with ice cooling, and the ether layer separated off after 15 min, the aqueous layer being extracted 6 times with hot benzene (I 1). The solvents were completely distilled off from the ether and benzene solutions, the crude carbinol being recrystallized from xylene, (after decolorizing the mother liquor with activated carbon.) Yield 13.5 g (76.7%), colorless crystals, mp 164^{ee.} Found: N 15.91, 15.94%. Calculated for C₁₀H₁₂N₂O: N 15.90%.

<u>1-Ethyl-2-methyl-5-hydroxymethylbenzimidazole (II)</u>. Prepared by the method described above from 23.2 g (0.1 mole) ethyl 1-ethyl-2-methylbenzimidazole-5-carboxylate [2] (in 300 ml dry ether) and 4.75 g (0.125 mole) lithium aluminum hydride (in 250 ml ether). Yield of carbinol II 14.3 g (75%). Colorless crystals mp 107-108°. Found: N 14.72, 14.73%. Calculated for $C_{11}H_{14}N_2O$: N 14.73%.

<u>1-Phenyl-2-methyl-5-hydroxymethylbenzimidazole (III)</u>. Synthesized in a way similar to that described above, starting from 14.0 g (0.05 mole) ethyl 1-phenyl-2-methylbenzimidazole-5-carboxylate [2] (in 320 ml dry ether) and 2.4 g (0.063 mole) lithium aluminum hydride (in 125 ml ether). The carbinol crystallized out when the benzene extract cooled. Concentration of the benzene mother liquor gave an additional quantity of carbinol suitable, without further purification, for preparation of aldehyde. Yield 10.2 g (85.7%). The pure carbinol formed colorless crystals, mp 174° (from benzene). Found: N 11.85, 11.91% Calculated for $C_{15}H_{14}N_2O$: N 11.76%.

Heating 0.5 g III with 3 ml methyl iodide at 100° in a sealed tube for 1 hr, gave the methiodide, washed with acetone. Yield almost theoretical. Colorless needle-shaped crystals, mp 228° (from alcohol). Found, I 33.71, 33.72%. Calculated for $C_{16}H_{17}IN_2O$: I 33.42%.

<u>1-Alkyl(or phenyl)-2-methyl-5-formylbenzimidazoles</u> (general synthetic method). A warm solution of 0.009 mole chromic anhydride in 8 ml 80% acetic acid was added, with stirring, to a hot solution of 0.01 mole 1-alkyl (or phenyl)-2-methyl-5-hydroxymethylbenzimidazole in 8 ml of the same solvent, after which the whole was refluxed for 1 hr, left for 2 hr, poured into about 40 ml of water and ice, made alkaline with 40% aqueous potassium hydroxide, and extracted 4-5 times with warm benzene (300-450 ml). The extract was dried over sodium sulfate, partly decolorized with active carbon, the solvent distilled off, and the crystalline residue recrystallized from 7-25 times its own quantity of xylene, or from a large quantity of ligroin petrol ether (bp 80-120°), the mother liquor being treated with decolorizing carbon.

1, 2-Dimethyl-5-formylbenzimidazole (IV). Colorless small crystals, mp 90-91° (from xylene). Yield after a single crystallization 46%. Found: N 15.97, 16.08%. Calculated for $C_{10}H_{10}N_2O$: N 16.09%.

 $\frac{1-\text{Ethyl-2-methyl-5-formylbenzimidazole (V). Colorless small crystals, mp 103-104° (from xylene). Yield after a single crystallization 43%. Found: N 14.79, 14.69%. Calculated for C₁₁H₁₂N₂O: N 14.88%.$

<u>1-Phenyl-2-methyl-5-formylbenzimidazole (VI)</u>. Colorless small needle-shaped crystals, mp 131° (from ligroin). Yield after a single crystallization 54%. Found: N 12.04, 12.08%. Calculated for C₁₅H₁₂N₂O: N 11.86%.

The methiodide of aldehyde VI was prepared by heating 0.47 g VI with 3 ml methyl iodide for 1 hr at 100° in a sealed tube. It was washed with acetone. Colorless needle-shaped crystal mp 252° (decomp. from alcohol). Yield 0.53 g (70%). Found: I 33.43, 33.46%. Calculated for $C_{16}H_{15}IN_2O$: I 33.59%.

The ethiodide of aldehyde VI was obtained by heating VI with excess ethyl iodide at 125° for 5 hr in a sealed tube. After washing with acetone and recrystallizing from alcohol, it formed colorless small crystals mp 226-227°.

<u> β -[1-alkyl (or phenyl)-2-methylbenzimidazolyl-5]acrylic acid (general synthetic method)</u>. A mixture of 1-alkyl (or phenyl)-2-methyl-5-formylbenzimidazole and malonic acid, about 4 mmole of each, together with 1 ml α -picoline, was heated on a water bath for 4 hr in a flask fitted with a reflux air condenser. After cooling, the crude benzimidazolyl-acrylic acid was washed with ether, taken up in warm 10% aqueous sodium carbonate, the solution decolorized with ac-tive carbon, made neutral with 15% acetic acid, and the precipitate washed with water, dried, and recrystallized from alcohol.

<u>β-(1, 2-dimethylbenzimidazolyl-5)acrylic acid (VIII)</u>. Colorless small needle-shaped crystals, mp 293-295° (decomp). Yield after crystallizing 51%. Found: N 12.74, 12.76%. Calculated for C₁₂H₁₂N₂O₂: N 12.96%.

^{*}Mps of new compounds are corrected.

<u>β-(1-ethyl-2-methylbenzimidazolyl-5)acrylic acid (VIII)</u>. Colorless small crystals, mp 253-254° (decomp). Yield after crystallizing 50%. Found: N 12.01, 12.24%. Calculated for C₁₃H₁₆N₂O₂: N 12.17%.

 $\frac{\beta - (1 - \text{phenyl} - 2 - \text{methylbenzimidazolyl} - 5)\text{acrylic acid (IX)}. \text{ Colorless glistening transparent needles, mp 287°.}$ Yield after crystallizing 49%. Found: N 10.21, 10.00%. Calculated for C₁₇H₁₄N₂O₂: N 10.08%.

The methiodide of acid IX formed colorless needles, mp 302° (decomp, from alcohol). Found: I 29.96; N 6.74%. Calculated for C₁₈H₁₇IN₂O₂: I 30.23% N 6.66%.

Heating acid IX with excess ethyl iodide for 4 hr at 125° in a sealed tube gave a 50% yield of the ethiodide of IX, forming colorless crystals mp 203° (from alcohol). Found: N 6.59, 6.78%. Calculated for $C_{19}H_{19}I_{N2}O_2$: N 6.45%.

3-Ethyl-5-[1'-alkyl (or phenyl)-2'-methylbenzimidazolyl-5']methylenerhodanines (general method of preparation). A mixture of 3 mmole 1-alkyl (or phenyl)-2-methyl-5-formylbenzimidazole, 0.48 g (3 mmole) 3-ethylrhodanine, and 0.5 ml dry pyridine was refluxed for 30 min. After cooling, 5 ml methanol was added, the yellow precipitate filtered off, washed with a small amount of methanol, and recrystallized from that solvent. In the case of 1-phenyl-2-methyl-5-formylbenzimidazole, 1.5 ml water was added to the crude condensation product from 3-ethylrhodanine, and after an hour the precipitate filtered off, washed with 50% aqueous pyridine, and recrystallized from 70% pyridine.

<u>3-Ethyl-5-(1', 2'-dimethylbenzimidazolyl-5')methylenerhodanine (X)</u>. Pale yellow needle-shaped crystals mp 215-216°. Yield 63%. Found: S 19.96, 19.98%. Calculated for C₁₅H₁₅N₃OS₂: S 20.18%.

 $\frac{3-\text{Ethyl-5-(1'-ethyl-2'-methylbenzimidazolyl-5')methylenerhodanine (XI)}{75.5\%}$ Small yellow crystals mp 182-183°. Yield 75.5% Found: S 19.26, 19.15%. Calculated for C₁₆H₁₇N₉OS₂: S 19.33%.

<u>3-Ethyl-5-(1'-phenyl-2'-methylbenzimidazolyl-5')methylenerhodanine (XII)</u>. Golden yellow needle-shaped crystals mp 182°. Yield 75%. Found: S 17.05, 17.13%. Calculated for C₂₀H₁₇N₃OS₂: S 16.88%.

Methiodide of base XII: this formed small pale yellow crystals mp 280-282°. Yield 75%. Found: I 24.30, 24.12%. Calculated for $C_{21}H_{20}IN_3OS_2$: I 24.37%.

<u>3-Ethyl-5-{[1'-phenyl-3'-ethyl-5'formybenzimidazolinylidene-2']ethylidene}</u> rhodanine (XIII). A mixture of 0.39 g (1 mmole) aldehyde VI ethiodide, 0.3 g (1 mmole) 3-ethyl-5-acetanilidomethylenerhodanine, 5 ml dry pyridine, and 0.3 ml triethylamine was refluxed for 45 min. After 24 hr the precipitate of dye was filtered off, washed with methanol and ether, and recrystallized from 15 ml ethanol. If formed a dark red powder with a greenish metallic reflex, mp 243°, λ_{max} 525 mµ^{*}. Yield 25%. Found: N 9.72, 9.58; S 14.54, 14.46%. Calculated for C₂₃H₂₁N₃O₂S₂: N 9.65; S 14.71%.

<u>3-Ethyl-5-{[1'-phenyl-3'ethyl-5'-(B-carboxyvinyl)benzimidazolinylidene-2]ethylidene}</u>-rhodanine (XIV). A mixture of 0.65 g (1.5 mmole) ethiodide of acid IX, 0.46 g (1.5 mmole) 3-ethyl-5-acetanilidomethylenerhodanine, 10 ml dry alcohol, 0.5 ml triethylamine was refluxed for 1 hr. 5 ml hot water was added to the hot solution, and the whole allowed to stand for 24 hr. The precipitate of dye was filtered off, washed with ether, dried, and chromatographed (absorbent Al₂O₃, eluant chloroform). Dark red finely-divided crystalline powder, mp 190°, λ_{max} 527 mµ. Yield 0.1 g (15%). Found: N 8.74, 8.66% Calculated for C₂₅H₂₃N₃O₃S₂: N 8.80%.

<u>1, 1'-Diphenyl-3, 3'dimethyl-5, 5'-diformylimidocarbocyanine iodide (XV)</u>. A mixture of 0.76 g (2 mmole) methiodide of aldehyde VI, 10 ml nitrobenzene, and 1 ml orthoformic ester was heated for 1 hr in a bath at 190°. The dye was then precipitated with ether, washed with the same solvent, and recrystallized from 55 ml alcohol. Dark, finelydivided crystalline powder with a slight metallic reflex, mp 215°; λ_{max} 521 mµ. Yield 0.13 g (10%). Found: N 8.68, 8.70%. Calculated for $C_{33}H_2 IN_4O_2$: N 8.77%.

<u>1</u>, 1'-Diphenyl-3, 3'-diethyl-5, 5'-di(β -carboxyvinyl)imidocarbocyanine iodide (XVI). Prepared similarly to the preceding compound, using 0.65 g (1.5 mmole) ethiodide of acid IX, 8 ml nitrobenzene, and 1 ml orthoformic ester. After precipitation with ether, the dye was washed with water, dried, and recrystallized from 8 ml ethanol. Dark reddish finely-divided crystalline powder, mp 263° (decomp), λ_{max} 537 mµ. Yield 0.17 g (15.5%). Found: I 16.71, 16.58%. Calculated for C₃₉H₃₅IN₄O₄: I 16.93%.

REFERENCES

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2. V. M. Zubarovskii, R. N. Moskaleva, and M. P. Bachurina, ZhOKh, 32, 1581, 1962.

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^{*}The chief absorption maxima for dyes XIII-XVI were determined in ethanol solution, using a SF-10 spectrophotometer.