THE ALKYLATION OF BENZIMIDAZOLE DERIVATIVES WITH γ-VALEROLACTONE

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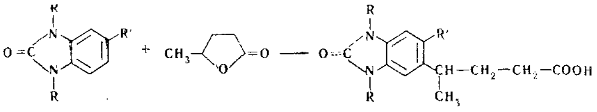
Reaction of 1,3-dimethylbenzimidazolone and its 5-methyl and 5-chloro derivatives with γ-valerolactone in presence of anhydrous aluminum chloride gives the corresponding 6-(1'-methyl-3'-carboxypropyl)-benzimidazolones.

In continuation of our work on the alkylation of benzimidazolones with γ-butyrolactone [1], the condensation of 1,3-dimethylbenzimidazolone (I) and its 5-methyl (II) and 5-chloro (IV) derivatives with γ-valerolactone has been carried out in order to synthesize potential growth regulants, and substances which increase the resistance of cotton to wilting.


I-IV R=H, CH$_3$ R'=H, CH$_3$, Cl V-VIII

As would be expected, condensation of 5-chlorobenzimidazolone (III) and its 1,3-dimethyl derivative (IV) with γ-valerolactone takes place in the presence of a large excess of aluminum chloride to give low yields in comparison with I and II. In agreement with the literature [2, 4], alkylation of I–IV occurs at the 6(5)-position of the benzene ring. The possibility of alkylating benzimidazolones depends to a large extent on steric factors. Apparently as a result of steric hindrance, it proved impossible to alkylate 1,3-dimethyl-5-t-butylbenzimidazolone with γ-valerolactone. This is in agreement with the known impossibility of o-alkylating tert-butylbenzene with alkyl halides [5] or γ-lactones [6].

The IR spectra of V–VIII show absorption bands due to the CO of the benzimidazolone ring and of the carboxyl group (1670–1685 and 1715–1725 cm^{-1}), and also bands corresponding to 1,2,3- and 1,2,4,5-substituted benzene rings (810–820 and 850–855 cm^{-1}) [7]. The NMR spectra (recorded on a JNM 4H-100 instrument with a working frequency of 100 MHz, using CF_3COOH as solvent and tetramethylsilane as standard, δ scale) of V–VIII show a clear doublet at high field due to the CH_3 group, at δ 1.25–1.72 ppm. The methylene group in the β-position to the carboxyl group gives rise to a two-proton doublet at 2.4–2.6 ppm, and the methylene group in the α-position appears as a two-proton triplet at 2.1–2.3 ppm. The protons of the N–CH_3 group appear clearly at δ 3.7–3.9 ppm.

EXPERIMENTAL

1,3-Dimethylbenzimidazolone (I) and its derivatives were obtained by the methods given in [4, 8].

1,3-Dimethyl-5-(1'-methyl-3'-carboxypropyl)benzimidazolone (V). To a mixture of 4.1 g (0.025 mole) of I and 2.5 g (0.025 mole) of γ-valerolactone in 150 ml of tetrachloroethylene was added in small portions 10 g (0.075 mole) of anhydrous aluminum chloride, and the mixture was heated on the boiling water bath for 2 hr. It was then cooled, and poured into a mixture of 25 ml of conc HCl acid and ice. The tetrachloroethylene was removed in a current of steam, and the residual dark brown oil, after cooling, was dissolved in sodium bicarbonate solution, charcoaled, and acidified with conc HCl. Part of the material separated as an oil, and crystalline product separated from the acid filtrate on standing. The reaction product was extracted in a crystalline state from the oil only by three repetitions of this procedure. The yield was 3.4 g (53%), mp 138–139° C (from aqueous ethanol).

Compounds VI–VIII were obtained similarly (see table). Benzimidazolones II–IV were reacted with γ-valerolactone in equimolecular amounts. The methyl esters (see table) were obtained by treating V–VIII with diazomethane.

6-(1'-Methyl-3'-carboxypropyl)benzimidazolones (V–VIII)

Compound	R	R′	Yield, %*	Mp, °C	Found, %			Calculated, %			Molecular formula	λ_{max}, nm (lg)***	Methyl ester, mp, °C
					C	H	N	C	H	N			
V	CH_3	H	53 (3)**, 37 (2.8), 0 (2.4)	138—139	64.0	6.8	10.5	64,1	6,8	10.6	$C_{14}H_{18}N_2O_3$	235 (3.86), 287 (3.93)	45—46
VI	CH_3	CH_3	56 (3), 38 (2.8), 5 (2.4)	130—131	65.1	7.3	10.1	65.2	7,2	10.1	$C_{15}H_{20}N_2O_3$	237 (3.84), 293 (3.93)	63—64
VII	H	Cl	15 (3.5)**	232—233	53.5	5.0	10.2	53.0	4,8	10.4	$C_{12}H_{13}ClN_2O_3$	237 (3.84), 297 (3.95)	163—164
VIII	CH_3	Cl	15 (3.5)**	141—142	56.5	5.8	9.4	56.6	5,7	9.4	$C_{14}H_{17}ClN_2O_3$	239 (3.85), 293 (3.97)	49—50

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*The amount of $AlCl_3$ per mole of reactant is given in parentheses.

**At 120°, the yield of V was 23%, and of VII and VIII, 15%.

***Conditions for recording of spectra: solvent, concentration, apparatus.

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