5,6-DIHYDRO-4H-IMIDAZO[4,5,1-i,j]QUINOLINE DERIVATIVES

II.* SYNTHESIS AND TRANSFORMATION OF 2-FORMYL DERIVATIVES

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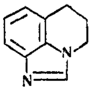
The oxidation of 2-hydroxymethyl and 2-methyl derivatives of 5,6-dihydro-4H-imidazo-[4,5,1-i,j]quinoline with active manganese dioxide and selenium dioxide gave 2-formyl derivatives of this heterocycle. Some transformations of these compounds are realized.

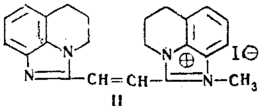
Compounds of the 5,6-dihydro-4H-imidazo[4,5,1-i,j]quinoline (I) series can be considered to be 1,7-trimethylenebenzimidazole derivatives. A study of some of them demonstrated that the inclusion of a trimethylene bridge in the benzimidazole molecule alters the properties of the latter comparatively slightly. Thus the oxidation of 2-hydroxymethyl- and 2-methyl-substituted I to the previously undescribed formyl derivatives proceeds almost as smoothly as in the benzimidazole series [2-4].

2-Hydroxymethyl-substituted I are oxidized by the action of freshly sublimed selenium dioxide in aqueous dioxane to give 70-90% of the corresponding aldehydes; the reaction with active manganese dioxide [5,6] in chloroform proceeds with somewhat greater difficulty. As in the case of benzimidazole [4], the oxidation of 2-methyl-substituted I with selenium dioxide in absolute dioxane or toluene results in lower yields of the formyl derivative. An exception to this is the 2,9-dimethyl derivative of I, which gives 72% of the aldehyde in absolute dioxane.

The compounds that we obtained were subjected to some reactions that proceed readily with 2-formyl derivatives of benzimidazole. For example, in the presence of piperidine the 2-formyl derivative of I (III) condenses with the methiodide of the 2-methyl derivative of I to give a high yield of II. In the presence of alkali, III and its derivatives readily react with acetophenone and are thereby converted to 2-(β-benzoylvinyl) derivatives; however, in contrast to 1-methyl-2-formylbenzimidazole [3], they react with only one molecule of acetophenone (see Table 1).



I



II

EXPERIMENTAL

2-Hydroxymethyl- and 2-Methyl-Substituted I. A solution of 0.1 mole of the dihydrochloride of the 8-amino-1,2,3,4-tetrahydroquinoline derivative [1] and 0.15 mole of glycolic acid in 30 ml of water was refluxed for 6 h. The mixture was neutralized with ammonia, and the precipitated hydroxymethyl derivative of I was filtered and washed with water and ether. To obtain the 2-methyl-substituted derivatives of I, the dihydrochloride of the 8-amino-1,2,3,4-tetrahydroquinoline derivative was refluxed with acetic acid for 5 h.

Oxidation Procedures. A. A 1-g sample of the 2-hydroxymethyl derivative of I was dissolved in 50 ml of chloroform, 10 g of active manganese dioxide was added, and the mixture was shaken for 24 h. The resulting precipitate was filtered and washed with chloroform. The solvent was removed by distillation, and the aldehyde was chromatographed on aluminum oxide with elution by chloroform.

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*See [1] for communication I.

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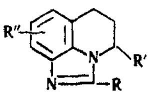
TABLE 1. 5,6-Dihydro-4H-imidazo[4,5,1-i,j]quinoline Derivatives



R	R′	R″	mp (crystal. solvent)	Empirical formula	Found %			Calc. %			Yield, %
					C	H	N	C	H	N	
CH_2OH	CH_3	8-CH_3	167—168 (butanol)	$C_{13}H_{16}N_2O$	72,4	7,3	13,1	72,2	7,5	13,0	98
CH_2OH	CH_3	8-CH_3O	179—180 (toluene)	$C_{13}H_{16}N_2O_2$	67,0	7,1	12,0	67,2	6,9	12.1	80
CH_2OH	H	9-CH_3	183—184 (ethyl acet.)	$C_{12}H_{14}N_2O$	71,2	6,7	14,0	71,2	7,0	13,9	99
CH_3	CH_3	8-CH_3	154—155 (petrol. ether)	$C_{13}H_{16}N_2$	77,7	8,1	14,0	77,9	8,1	14,0	80
CH_3	H	9-CH_3	150—151 (n-octane)	$C_{12}H_{14}N_2$	77,6	7,6	15,1	77,4	7,6	15,0	76
CHO	H	H	179—180 (aqueous alcohol)	$C_{11}H_{10}N_2O$	71,0	5,3	15,4	70,9	5,4	15,1	81 (A)*
CHO	CH_3	8-CH_3	102—103 (sublim.)	$C_{13}H_{14}N_2O$	73,2	6,7	13,1	72,9	6,6	13,1	66 (A)*
CHO	CH_3	8-CH_3O	136—138 (sublim.)	$C_{13}H_{14}N_2O_2$	67,7	6,0	12,4	67,8	6,1	12,2	58 (A)*
CHO	H	9-CH_3	111—112 (sublim.)	$C_{12}H_{12}N_2O$	72,2	6,2	14,1	72,0	6,1	14,0	62 (A)*
HC=NOH	H	H	255 (decom. alcohol)	$C_{11}H_{11}N_3O$	65,4	5,5	20,7	65,7	5,5	20,9	69
HC=NOH	CH_3	8-CH_3	163—164 (decomp. alcohol)	$C_{13}H_{15}N_3O$	67,9	6,7	18,3	68,1	6,6	18,3	80
HC=NOH	CH_3	8-CH_3O	140—141 (decomp. alcohol)	$C_{13}H_{15}N_3O_2$	63,5	6,1	17,2	63,6	6,2	17,1	92
HC=NOH	H	9-CH_3	156—157 (decomp. alcohol)	$C_{12}H_{13}N_3O$	67,0	6,3	19,3	66,9	6,1	19,5	93

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*The yields of aldehydes in oxidation by the other methods were as follows (in percent): R' =R" =H, 72 (method B), 15 (C), 10 (D); R' =R" =CH_3, 71 (B), 33 (C), 37 (D); R' =CH_3, R" =CH_3O, 70 (B), 48 (C), 38 (D); R' =H, R" =CH_3, 90 (B), 72 (C), 52 (D).

B. A 0.01 mole sample of the 2-hydroxymethyl derivative of I was dissolved by heating in 25 ml of absolute dioxane, and a solution of 0.005 mole of selenium dioxide in 10 ml of dioxane and 4 ml of water was added in small portions. The mixture was stirred at the boiling point for 2 h. The selenium was removed by filtration, the dioxane was removed by distillation, and the aldehyde was purified as in method A.

C. A 0.005 mole sample of the 2-methyl derivative of I and 0.005 mole of selenium dioxide in 20 ml of absolute dioxane was heated to the boiling point and refluxed for 2 h. Chloroform (50 ml) was then added, and the mixture was shaken with 20 ml of saturated sodium bisulfite solution. The chloroform layer was separated, the aqueous solution was neutralized with sodium carbonate, and the resulting aldehyde was filtered.

D. The oxidation was carried out as in method C in absolute toluene.

2-(β-Benzoylvinyl)-5,6-dihydro-4H-imidazo[4,5,1-i,j]quinoline (IV). A mixture of 0.56 g (3 mmole) of III, 0.72 g (6 mmole) of acetophenone, and 1 ml of alcohol was heated on a water bath, two drops of 2% potassium hydroxide was added, and the mixture was heated for 10 min and allowed to stand at room temperature for 1 h. The precipitate was filtered and washed with ether to give 0.61 g (70%) of pale-yellow plates with mp 208-209° (from butanol). Found %: C 78.9; H 5.7; N 10.0. $C_{19}H_{16}N_2O$. Calculated %: C 79.1; H 5.6; N 9.7.

2-(β-Benzoylvinyl)-9-methyl-5,6-dihydro-4H-imidazo[4,5,1-i,j]quinoline. This was similarly obtained in 74% yield from the 2-formyl-9-methyl derivative of I. The yellow plates melted at 179-180° (from butanol). Found %: C 79.2; H 6.0; N 9.4. $C_{20}H_{18}N_2O$. Calculated %: C 79.4; H 6.0; N 9.3.

2-Methyl-5,6-dihydro-4H-imidazo[4,5,1-i,j]quinoline Methiodide (V). A 1.72 g (0.01 mole) sample of the 2-methyl derivative of I was dissolved by heating in 3 ml of absolute benzene, 1.8 ml (0.03 mole) of methyl iodide was added, and the mixture was allowed to stand at about 20° for 2 h. The precipitate was filtered and washed with benzene to give 3 g (95%) of colorless plates with mp 249-250° (from alcohol–ether). Found %: N 9.0. $C_{12}H_{15}IN_2$. Calculated %: N 8.9.

1,2-Bis(5,6-dihydro-4H-imidazo[4,5,1-i,j]-2-quinolyl)ethylene Methiodide. A 0.18 g (1 mmole) sample of III and 0.31 g (1 mmole) of V were dissolved in 3 ml of alcohol, two drops of piperidine were added, and the mixture was refluxed for 1 h. The reaction product was precipitated with ether to give 0.32 g (66%) of olive-yellow prisms with mp 285-287° (decomp., from aqueous alcohol). Found %: N 11.8. $C_{23}H_{27}IN_4$. Calculated %: N 11.6.

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