IMIDAZOLONES

III.* ACYLATION OF 2,5(4)-SUBSTITUTED 4(5)-IMIDAZOLONES

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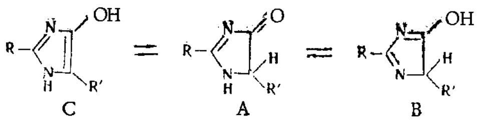
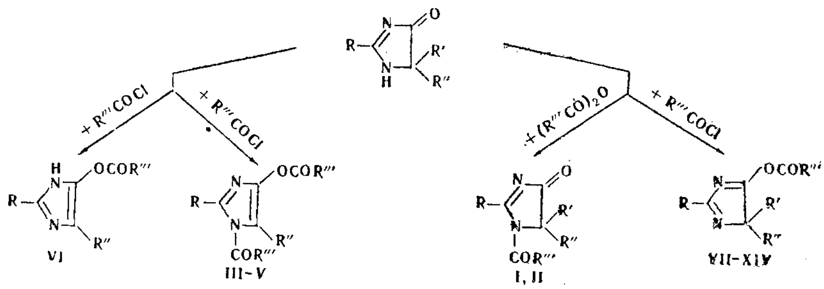
The reaction of 2,5(4)-substituted 4(5)-imidazolones with various acylating agents was studied, and it was established that the reaction medium, the nature of the acylating agent, and the substituent (R') in the 5(4)-position of the imidazole ring affect the acylation process.

2,5(4)-Substituted 4(5)-imidazolones are potential tautomers and may be found in several tautomeric forms that have different capacities for acylation.



According to the assertion of Chambon and Boucherle [2], the use of aliphatic and aromatic acid anhydrides as acylating agents gives N-acyl derivatives of 4(5)-imidazolone. This opinion does not agree with other data [3] in which the structures of O-acyl derivatives are assigned to the products of a similar reaction. Acid chlorides were used in [2] for the acylation of 4(5)-imidazolone, and diacyl derivatives are isolated in this case.

We have found that products with different structures – I, II, and III, IV, respectively, are obtained by the treatment of 5(4)-methyl-4(5)-imidazolones with carboxylic acid anhydrides and chlorides via the method in [2].



$R = C_6H_3(OCH_3)_2$-3',4'

I $R' = H$, $R'' = R''' = CH_3$; II $R' = H$, $R'' = CH_3$, $R''' = C_6H_5$; III $R'' = R''' = CH_3$; IV $R'' = CH_3$, $R''' = C_6H_5$; V $R'' = CH_3$, $R''' = p\text{-}NO_2C_6H_4$; VI $R' = H$, $R'' = CH_3$, $R''' = C_6H_5$; VII $R' = H$, $R'' = CH(CH_3)_2$, $R''' = CH_3$; VIII $R' = H$, $R'' = CH(CH_3)_2$, $R''' = C_6H_5$; IX $R' = H$, $R'' = CH(CH_3)_2$, $R''' = p\text{-}NO_2C_6H_4$; X $R' = H$, $R'' = CH_2CH(CH_3)_2$, $R''' = CH_3$; XI $R' = H$, $R'' = CH_2CH(CH_3)_2$, $R''' = C_6H_5$; XII $R' = H$, $R'' = CH_2CH(CH_3)_2$, $R''' = p\text{-}NO_2C_6H_4$; XIII $R' = R'' = CH_3$, $R''' = C_2H_5$; XIV $R' = CH_3$, $R'' = C_2H_5$, $R''' = C_6H_5$.

In the IR spectra of I and II, the absorption bands in the NH region vanish, and bands characteristic for the carbonyl group appear at 1715-1720 cm^{-1}; this makes it possible to consider these compounds to be N-acyl derivatives of 4-imidazolone. Absorption bands (two each) of ester (1785, 1760 cm^{-1}) and tertiary amide (1685, 1680 cm^{-1}) groups are observed in the IR spectra of III and IV.

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*See [1] for communication II.

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TABLE 1. Acyl Derivatives of 2,5(4)-Substituted 4(5)-Imidazolones

Comp.	Mp, °C	Empirical formula	Found,%		Calc.,%		Yield, %
			N, %	Mol. wt	N, %	Mol. wt	
I	178—179	$C_{14}H_{16}N_2O_4$	10,2	272	10,1	272,6	67
II	218—219	$C_{19}H_{18}N_2O_4$	8,2	341	8,3	338,2	74
III	141—142	$C_{16}H_{18}N_2O_5$	8,7	—	8,8	—	56
IV	208—210	$C_{26}H_{22}N_2O_5$	6,5	448	6,3	442,1	63
V	204—205	$C_{26}H_{20}N_4O_9$	10,3	—	10,5	—	48
VI	116—118	$C_{19}H_{18}N_2O_4$	8,4	336	8,3	338,2	51
VII	177—179	$C_{16}H_{20}N_2O_4$	9,1	—	9,1	—	74
VIII	197—198	$C_{21}H_{22}N_2O_4$	7,8	361	7,6	366,4	74
IX	189—191	$C_{21}H_{21}N_3O_6$	10,0	417	10,1	411,2	64
X	187—188	$C_{17}H_{22}N_2O_4$	8,9	—	8,8	—	92
XI	201—202	$C_{22}H_{24}N_2O_4$	7,4	388	7,4	380,2	88
XII	234—235	$C_{22}H_{23}N_3O_6$	9,7	423	9,9	425,4	93
XIII	166—168	$C_{22}H_{20}N_2O_4$	9,3	—	9,2	—	55
XIV	195—196	$C_{21}H_{22}N_2O_4$	7,7	—	7,7	—	58

Schotten–Baumann acylation of 5(4)-methyl-4(5)-imidazolone gave VI – a derivative of enol form B. The IR spectrum of VI contains a broad, weak band at 3400 cm^{-1} and a band with a maximum at 1740 cm^{-1} due to ester group vibrations. In addition to the above absorption bands, there are intense bands with a maximum at 1690 cm^{-1} associated with the development of an intramolecular hydrogen bond. In fact, the difference $\nu_{CO} - \nu_{CO...NH} = 1740 - 1690 = 50\ cm^{-1}$ is in complete agreement with the shift of the ester group absorption band to the low-frequency region during the formation of an intramolecular hydrogen bond [4,5].

Attempts to obtain O-acyl derivative form B via the method in [2] through the organomagnesium compound did not give the expected results; only N-acylation products (I, II) were isolated.

The results of the acylation of 4(5)-imidazolone containing an isopropyl or isobutyl group in the 5(4)-position were extremely peculiar. Monoacyl derivatives of form B were always isolated in these experiments when various acylating agents in various media (including Schotten–Baumann acylation) were used. The absorption bands in the NH and C=O regions vanish in the IR spectra of the compounds obtained (VII-XIV), and absorption bands characteristic for the ester group appear at 1745-1785 cm. Compounds XIII and XIV, for which the formation of form C is excluded and which we used as model compounds, are of special interest.

The anomalous behavior of 2-(3',4'-dimethoxyphenyl)-5(4)-isopropyl- or 5(4)-isobutyl-4(5)-imidazolones can apparently be explained by shielding of the reaction center at the 1-position by the bulky group in the 5(4)-position and also by the extremely low lability of the hydrogen in the 5(4)-position as a consequence of the positive inductive effect of the group.

EXPERIMENTAL

1-Acetyl-2-(3',4'-dimethoxyphenyl)-5-methyl-4-imidazolone (I). A total of 2.34 g (0.01 mole) of 2-(3',4'-dimethoxyphenyl)-5(4)-methyl-4(5)-imidazolone (XV) was refluxed in 10 ml (0.105 mole) of acetic anhydride for 30 min and cooled. The resulting crystals were filtered, washed with 10-15 ml of ether, and crystallized from 60% ethanol to give 1.85 g of I.

Compounds III, VII, VIII, X, XI, and XIV were similarly obtained. Dioxane was used as the solvent for acylation with benzoic anhydride.

1-Acetyl-2-(3',4'-dimethoxyphenyl)-5-methyl-4-acetoxyimidazole (III). Acetyl chloride [1.5 ml (0.02 mole)] was added to 2.34 g (0.01 mole) of XV in 8 ml of dry pyridine, and the mixture was refluxed on a water bath with vigorous stirring for 2 h. The crystals that formed on cooling were filtered and washed with ice water. The product was recrystallized twice from 70% ethanol to give 1.78 g of III.

Compounds IV, V, VII-XIV were similarly obtained.

2-(3',4'-Dimethoxyphenyl)-4-methyl-5-benzoyloxyimidazole (VI). A 2.34 g (0.01 mole) sample of XV was dissolved in 15 ml of 2% NaOH, 1.5 ml (0.012 mole) of benzoyl chloride was added to the solution with vigorous stirring, and the mixture was stirred at room temperature for 3 h. The oil that separated began to crystallize on standing for 24 h. The reaction product was filtered, washed with water, and crystallized from ethanol to give 1.72 g of VI.

Compounds X and XIV were similarly obtained.

The characteristics of the compounds obtained are presented in Table 1. The molecular weights were determined by the Rast method. The IR spectra of mineral oil suspensions were recorded with an IKS-12 spectrometer.

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