ketone), and an essentially unchanged ultraviolet absorption (λ_{max} 258, 291 mμ (log ε 3.82, 3.71)) demonstrating the new carbonyl to be unconjugated and located in a six-membered or larger ring.

The above observations lead to the conclusion that curcolone has the constitution I (without stereochemistry).

The NMR signal due to the C-1 hydrogen of curcolone appeared as a triplet (J=8 c.p.s.) which indicated the C-1 hydroxyl to be situated in a quasi-equatorial configuration. Application of the benzoate rule[4] showed that the absolute configuration at C-1 is *S*, the C-1 hydroxyl group being consequently α-oriented. Inspection of Dreiding models reveals that the C-10 methyl is located in an α-configuration, since only this arrangement can make the C-1 hydroxyl α- and equatorially situated. The combined evidence points to the stereostructure I for curcolone.

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Alkyl Migration of 3-Alkylguanine Derivatives

We have previously described the conversion of the 3-alkyl- and 3-glycosyladenine derivatives to the corresponding 9-isomers by heating with hydrogen halides or mercuric halides.[1~3] Acyl groups on N^6 of adenine were necessary for this migration reaction, while N^6-methyl and N^6,N^6-dimethyl[4] were not so effective. It was expected that the other 3-alkylpurines with proper electron-withdrawing substituents on the pyrimidine segment underwent the analogous migration reaction. The present paper deals with the migration of benzyl group on N-3 of N^2-acetylguanine toward the N-7 and N-9 positions, and with the direct benzylation and ribosylation of N^2-acetylguanine.

3-Benzyl-N^2-acetylguanine (II) was prepared by acetylation of 3-benzylguanine (I) which was synthesized *via* 3-benzyl-3,6-dihydro-2-methylthio-6-oxo-9*H*-purine by a similar method described for 3-methylguanine.[5] Deacetylation of II recovered 3-benzylguanine (I), whose structure was confirmed in comparison of ultraviolet absorption spectra with those of 3-methylguanine.[5,6] Benzyl migration occurred when HBr salt of II was heated at 120~130° for 20 hours in N,N-dimethylacetamide (DMA) giving rise

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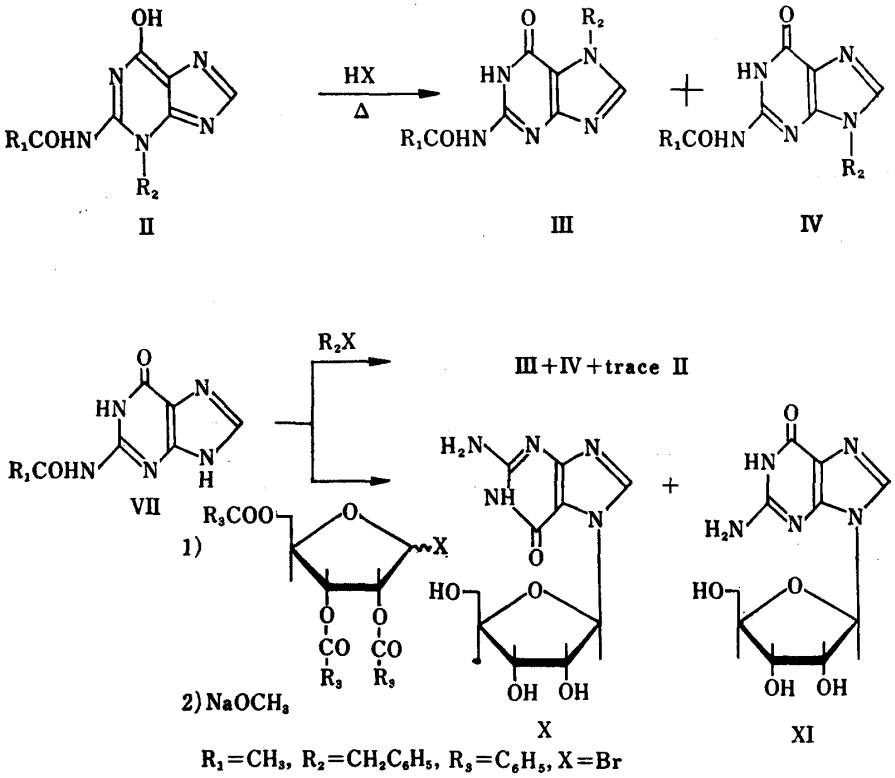

Chart 1.

to 7-benzyl-N^2-acetylguanine (Ⅲ) (28% yield) and 9-benzyl-N^2-acetylguanine (Ⅳ) (30%). Treatment of Ⅲ and Ⅳ with sodium methoxide afforded 7-benzylguanine (Ⅴ) and 9-benzylguanine (Ⅵ). Ultraviolet absorption spectra and pKa values of the compounds were similar to those of the corresponding methylguanines.[7]

When a solution of equimolar amounts of Ⅱ-HBr and N^2-acetylguanine-8-^{14}C (13.4×10^9 d.p.m./mole) in DMA was heated at 120~130° for 20 hours, 7- and 9-benzyl-N^2-acetylguanine formed were found to have 53% (7.1×10^9 d.p.m./mole) and 56% (7.5×10^9 d.p.m./mole) of the specific radioactivity of N^2-acetylguanine-8-^{14}C, respectively. The radioactivity of the recovered N^2-acetylguanine was reduced to 46% (6.2×10^9 d.p.m./mole). The dilution of radioactivity indicated that the migration reaction proceeded by an intermolecular mechanism.

Direct condensation of N^2-acetylguanine (Ⅶ) with benzyl bromide in DMA at 90° for 7 hours gave mainly 7- (Ⅲ) (22% yield) and 9- (Ⅳ) (16%) benzyl-N^2-acetylguanine, but only a trace amount of the 3-isomer (Ⅱ) (0.2%) was obtained. Coupling of Ⅶ and 2,3,5-tri-O-benzoyl-D-ribofuranosyl bromide in DMA at 60° for 40 hours gave 7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-N^2-acetylguanine (Ⅷ) (25% yield) and the 9-β-isomer (Ⅸ) (23%).*[1] Treating the products (Ⅷ and Ⅸ) with sodium methoxide afforded 7-β-D-ribofuranosylguanine[8] (Ⅹ) [NMR*[2]: $H_{1'}=6.04$ p.p.m. (doublet, J=5.3 c.p.s.) $[\alpha]_D^{20}$ −17°(c=1.0 in 0.1*N* NaOH)] and the 9-β-isomer (Ⅺ), the latter was identical with the authentic sample of guanosine. The properties of the compounds thus obtained are shown in Table I.

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Table I. Properties of Substituted Guanines

Substituents	No.	m.p.[a] (°C)	λ_{max} mμ ($\varepsilon \times 10^{-3}$)[b] pH 1	pH 7	pH 13	pKa[c]
3-Benzyl-N^2-acetyl	II	285	265 (13.5)	227 (15.1) 270 (14.9)	229 (15.8) 276.5(15.5)	
7-Benzyl-N^2-acetyl	III	241	263.5(19.4)	222 (21.8) 265 (15.9)	222.5(26.8) 269 (11.7)	
9-Benzyl-N^2-acetyl	IV	229	263 (20.8)	261 (19.1) [283 (11.7)]	264 (14.2)	
3-Benzyl	I	340	[243 (8.2)] 263 (12.5)	236 (11.1) 268.5(12.9)	274 (14.2)	4.00 9.70
7-Benzyl	V	>380 (decomp.)	251 (11.6) [275 (7.1)]	248 (6.6) 284.5(7.3)	[242 (7.5)] 281.5(7.4)	3.47 9.85
9-Benzyl	VI	304	255.5(13.3) 279 (8.8)	253 (14.1) [272 (10.3)]	[258 (10.9)] 268.5(11.6)	2.84 9.82
7-β-D-Ribofuranosyl	X	250 (decomp.)	249.5(10.3) [271 (7.2)]	244 (6.7) 286 (7.9)	[240 (7.6)] 282 (6.9)	2.89 9.46
	VII	amorph.	(EtOH)	225.5(52.4) 275 (15.3)	265.5(16.5) 283 (13.3)	
	IX	amorph.	(EtOH)	231 (46.5) 260 (19.4) 282 (14.7)	252.5(20.6) 275 (15.1)	

a) Uncorrected [ ]=Inflection *b*) Determined in H_2O (decomp.)=Decomposed *c*) Determined spectrophotometrically in H_2O

These results indicate that 7- and 9-substituted N^2-acetylguanines are thermodynamically more stable than the 3-isomers, whereas the frontier[9] electron density of N-3 of N^2-acetylguanine was found to be greater than that of N-7 and N-9 in calculation by simple LCAOMO method. Under the above conditions the 3-isomers are assumed to be initially formed and rapidly converted to the 7- and 9-isomers. Further investigation on other derivatives besides adenine and guanine is in progress. Recently, the conversion of 1,3-dibenzylhypoxanthine to the 1,7- and 1,9-isomers has been reported.[10] Analogous migration reactions of many other biologically interesting 3-substituted purines will be found in the future.

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