Cyclonucleosides Related to Adenosine and Tubercidin

Kentaro ANZAI and Masanao MATSUI

The Institute of Physical and Chemical Research, Wako-shi, Saitama

Received August 11, 1972

Treatment of N⁶,N⁶-dibenzoyl-2',3'-O-isopropylidene-5'-O-mesyladenosine (IV) with an equimolar amount of sodium hydroxide afforded a cyclonucleoside, IX, which was further converted to an imidazole cyclonucleoside, VI, with excess sodium hydroxide. In aqueous acetic acid VI was converted to a cyclonucleoside, XIII, which suffered from further degradation on mild alkaline hydrolysis giving a cyclonucleoside, XIV. In the tubercidin (7-deazaadenosine) series the reaction proceeded analogously.

A few 3,5'-anhydro derivatives of adenosine have already been known,^{7~9)} and all of them possess a tertiary immonium structure pairing with sulfonate anions (*e.g.* III). Analogously a 3,5'-cyclonucleoside of tubercidin¹⁾ (7-deazaadenosine)^{2,3)} was prepared.³⁾ We wish to report here novel 3,5'-cyclonucleosides related to adenosine and tubercidin which do not possess an ionic structure.

It was reported that the reaction of 2',3'-O-isopropylidene-adenosine (I) with tosyl chloride afforded 2',3'-O-isopropylidene-5'-O-tosyladenosine (II),^{4,5,8)} which was converted to a cyclonucleoside tosylate, III, in hot acetone.⁸⁾ We previously found that the conversion to III occurred on keeping II in a desiccator⁶⁾ and supposed that the cyclonucleoside formation might be suppressed if the base moiety of II was acylated. Mesylation and subsequent benzoylation of I were carried out without isolating the possible intermediate, 2',3'-O-isopropylidene-5'-O-mesyladenosine, to give N⁶, N⁶-dibenzoyl-2',3'-O-isopropylidene-5'-O-mesyladenosine (IV). Similarly N⁶, N⁶-ditoluoyl compound V was prepared.

The fact that NMR of V shows a six proton singlet at δ 2.32 attributable to two methyls of the toluoyl group and a pair of four proton doublets at δ 7.13 and δ 7.74 ($J=8$ Hz) suggests that both toluoyl residues of V are bound at N⁶ and rotate freely around the bond between N⁶ and C-6. Thus another possible assignment for IV and V to have N⁶, 1-diacyl

structure will not be taken here.*

Treatment of IV with sodium hydroxide (more than two equivalents) in methanol afforded a cyclonucleoside, VI. The NMR spectrum of VI exhibits a characteristic feature of the cyclonucleosides showing signals of ABX type attributable to unequivalent methylene protons at C-5'. A signal corresponding to the hydrogen at C-2 of the starting material (IV) is lacking. The mass spectrum exhibits the parent peak at m/e 383 as well as an intense peak at m/e 242, which is attributable to a fragment ion, VIII. On the contrary the reaction hardly proceeded in acetone with excess sodium hydroxide. Ditoluoyl derivative V was also converted to a N⁶-toluoyl cyclonucleoside, VII.

When IV was treated with an equimolar amount of sodium hydroxide, two products were obtained, the minor one being VI. The main product is also a cyclonucleoside, the NMR spectrum of which shows that two protons at C-5' are unequivalent. The assignment that it is a cyclonucleoside, IX, rather than a dehydrated compound, X taking one mole of crystalline water, is supported by the following observations. The analytical data shows that the molecular formula is C₂₀H₁₉N₅O₄ from which water is never lost on prolonged heating *in vacuo*. The mass spectrum exhibited the parent ion corresponding to IX, and further fragmentations, *e.g.* M⁺-CO-NH-

* Further proof for this assignment will be announced soon.

$\text{HCOH}\cdot\text{NCH}_2$, are explicable based on the structure, IX. A ion species corresponding to X was not detected. Moreover compound IX is benzoylated to give an ester, XI.

Compound IX was heated in aqueous acetic acid. TLC monitoring showed that rapid formation of a product was attended by its further degradation, and this initially formed product was isolated. The molecular formula, $\text{C}_{20}\text{H}_{20}\text{N}_4\text{O}_4$, shows that one nitrogen is lost from IX, and the reaction may proceed as shown in Chart 1 to give a 4-aminoimidazole cyclonucleoside, XIII. Mild alkaline hydrolysis of XIII afforded a cyclonucleoside, XIV.

In the tubercidin series the reactions proceeded analogously. Treatment of N^6 , N^6 -dibenzoyl-2',3'-O-isopropylidenetubercidin (XV)⁶⁾ with an equimolar amount of sodium hydroxide afforded a cyclonucleoside, XVI, which was further converted to a cyclonucleoside, XVII, in alkaline solutions. The mass spectrum of XVII shows the parent peak as well as a peak corresponding to a fragment, XVIII, and that of XVI gives a peak corresponding to XIX. Treatment of XVI with aqueous acetic acid afforded a cyclonucleoside, XX.

Previously we reported that XV reacted with sodium iodide to give three products, two of them being identified as iodides, XXI and XXII. Another minor product was announced to have the molecular formula of

$\text{C}_{21}\text{H}_{21}\text{N}_3\text{O}_6$ and the loss of one nitrogen atom from the starting material was hardly explained. Now this compound was shown to be identical with XX. Possibly the reaction path involves the initial formation of XVI and

its further degradation affording XX under acidic reaction conditions.

EXPERIMENTAL

*N*⁶, *N*⁶-Dibenzoyl-2',3'-*O*-isopropylidene-5'-*O*-mesyladenosine (IV). 2',3'-*O*-Isopropylideneadenosine (2.20 g, 7.18 mm) was suspended in anhydrous pyridine (50 ml) cooled at $-10^{\circ}\sim -20^{\circ}\text{C}$ and methanesulfonyl chloride (1.0 g, 8.23 mm) was added dropwise. After a clear solution was obtained, it was left at 0°C for 3 hr and benzoyl chloride (5.0 g, 35.5 mm) was added dropwise keeping the temperature below 5°C . The solution was kept in a refrigerator overnight and was poured onto an ice-cooled aqueous solution of sodium bicarbonate. The product was extracted with chloroform and was chromatographed on silicic acid with a mixture of benzene and ethyl acetate (2:1) to give a syrup, which was shown to be homogeneous on TLC, yield 2.56 g; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 270 (shoulder, 15400) and 248 (21300); $[\alpha]_{\text{D}}^{24} -13.4$ ($c=1.6$, CHCl_3); NMR (60 MHz, CDCl_3) δ : 1.37, 1.60 (two singlets, 6H, two isopropylidene methyls) and 2.85 (s, 3H, CH_3SO_3).

Found: C, 56.71; H, 4.73; N, 11.35; S, 5.10%. Calcd. for $\text{C}_{28}\text{H}_{27}\text{N}_5\text{O}_8\text{S}$: C, 56.65; H, 4.59; N, 11.80; S, 5.40%.

*N*⁶, *N*⁶-Di-*p*-toluoyl-2',3'-*O*-isopropylidene-5'-*O*-mesyladenosine (V). 2',3'-*O*-Isopropylideneadenosine (1.10 g, 3.59 mm) was treated with mesyl chloride (500 mg, 4.1 mm) and subsequently with *p*-toluoyl chloride (2.8 g, 18 mm) as described in the preceeding section. The product was chromatographed on silicic acid with a mixture of benzene and ethyl acetate (2:1), and crystallized from carbon tetrachloride, yield 1.53 g (70%); mp $81\sim 84^{\circ}\text{C}$; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 275 (shoulder, 29200) and 260 (32600); $[\alpha]_{\text{D}}^{24} -10.7$ ($c=1.65$, CHCl_3); NMR (100 MHz, CDCl_3) δ : 1.38, 1.60 (two singlets, 6H, two isopropylidene methyls), 2.32 (s, 6H, $2\text{CH}_3\text{C}_6\text{H}_4\text{CO}$), 2.86 (s, 3H, CH_3SO_3), 6.19 (d, 1H, H-1', $J_{1',2'}=2\text{Hz}$), 7.13 and 7.74 (d, 8H, $2\text{CH}_3\text{C}_6\text{H}_4\text{CO}$, $J_{\text{ortho}}=8\text{Hz}$). Found: C, 57.30; H, 4.95; N, 10.64; S, 4.97%. Calcd. for $\text{C}_{30}\text{H}_{31}\text{N}_5\text{O}_8\text{S}$: C, 57.96; H, 5.30; N, 11.27; S, 5.16%.

*N*⁵,5'-Anhydro-5-amino-4-(*N*-benzoylamidino)-1-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)imidazole (VI). (a) A solution of IV (297 mg, 0.5 mm) dissolved in a mixture of methanol (50 ml) and 0.1 N NaOH (15 ml) was heated at $60\sim 70^{\circ}\text{C}$ for 1 hr. The solution was concentrated and the product was extracted with chloroform. Evaporation of the chloroform afforded 122 mg of the residue, which was almost homogeneous on TLC. To prepare an analytical sample, the product was subjected to silicic acid chromatography with ethyl acetate and was crystallized from ethyl acetate and ligroin, mp 252°C ; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 335 (17800), 268 (16500) and 247 (16600); $[\alpha]_{\text{D}}^{24} +66.5$ ($c=2.18$, CHCl_3);

NMR (100 MHz, DMSO-*d*) δ : 1.32, 1.46 (two singlets, 6H, two isopropylidene methyls), 3.74 (broad d, 1H, H_a-5', $J_{\text{gem}}=15\text{Hz}$, the signal of H_b-5' is not analyzable because of the overlapped HDO signal at 3.30), 4.62, 4.99 (a pair of doublets, 2H, H-2' and H-3', $J_{2',3'}=6\text{Hz}$), 4.63 (broad, 1H, H-4'), 6.17 (s, 1H, H-1'), 7.65 (s, 1H, $-\text{N}=\text{CH}-\text{N}<$) and 7.3 $\sim$ 8.2 (complex, 5H, $\text{C}_6\text{H}_5\text{CO}$). Found: C, 59.78; H, 5.62; N, 18.09%. Calcd. for $\text{C}_{19}\text{H}_{21}\text{N}_5\text{O}_4$: C, 59.52; H, 5.52; N, 18.27%.

(b) A solution of IX (41 mg, 0.1 mm) in a mixture of methanol (10 ml) and 0.1 N NaOH (1 ml) was heated at $60\sim 70^{\circ}\text{C}$ for 1 hr and the product was isolated as described in (a). Silicic acid chromatography afforded 15 mg of VI.

*N*⁵,5'-Anhydro-5-amino-4-(*N*-*p*-toluoylamidino)-1-(2,3-*O*-isopropylidene- β -D-ribofuranosyl)imidazole (VII). A solution of V (621 mg, 1 mm) in a mixture of methanol (20 ml) and 0.5 N NaHCO_3 (5 ml) was refluxed for 4 hr, and after the evaporation of methanol the residue was extracted with chloroform. Silicic acid chromatography afforded an analytical sample, which was crystallized from benzene, yield 216 mg; mp $245\sim 247^{\circ}\text{C}$ (dec.); $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 333 (16800) and 270 (18500); $[\alpha]_{\text{D}}^{24} +132$ ($c=1.36$, CHCl_3); NMR (100 MHz, CDCl_3) δ : 1.36, 1.57 (two singlets, 6H, two isopropylidene methyls), 2.42 (s, 3H, $p\text{-CH}_3\text{C}_6\text{H}_4\text{CO}$), 3.44 (2H, complex, H-5'), 4.63, 5.02 (a pair of doublets, 2H, H-2' and H-3'), 4.72 (complex, 1H, H-4') and 5.92 (s, 1H, H-1'). Found: C, 60.13; H, 5.79; N, 17.75%. Calcd. for $\text{C}_{20}\text{H}_{23}\text{N}_5\text{O}_4$: C, 60.44; H, 5.83; N, 17.62%.

3,5'-Anhydro-*N*⁶-benzoyl-2',3'-*O*-isopropylideneadenosine hydrate (IX). A solution of IV (297 mg, 0.5 mm) dissolved in a mixture of methanol (50 ml) and 0.1 N NaOH (5 ml) was heated at $60\sim 70^{\circ}\text{C}$ for 1 hr. The solution was concentrated and the product was extracted with chloroform. Concentration of the organic layer to dryness afforded 166 mg of a solid, which was shown by TLC to be a mixture of two compounds. They were separated by silicic acid chromatography with ethyl acetate, and the less polar compound was found to be VI, yield 3 mg. The main product was eluted later from the column and was crystallized from ethyl acetate and ligroin, yield 53 mg; mp 245°C ; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 307 (15200) and 263 (14500); $[\alpha]_{\text{D}}^{24} -145$ ($c=0.5$, DMSO); NMR (100 MHz, DMSO-*d*) δ : 1.27, 1.45 (two singlets, 6H, two isopropylidene methyls), 3.07 (broad d, 1H, H-5_a', $J_{\text{gem}}=14\text{Hz}$), 4.89 (broad d, 1H, H-5_b', $J_{\text{gem}}=14\text{Hz}$), 4.57, 5.04 (a pair of doublets, 2H, H-2' and H-3', $J_{2',3'}=6\text{Hz}$), 4.76 (complex, 1H, H-4'), 6.25 (s, 1H, H-1'), 7.3 $\sim$ 8.1 (complex, 5H, $\text{C}_6\text{H}_5\text{CON}=\text{}$), 8.08 and 8.42 (two singlets, 2H, $-\text{N}=\text{CH}-\text{N}<$ and $-\text{HN}-\text{HCOH}-\text{N}-$); Mass m/e : 411 (M^+), 383 ($\text{M}^+ -\text{CO}$), 310 ($\text{M}^+ -\text{CO}-\text{NH}\cdot\text{HCOH}\cdot\text{NCH}_2$). Found: C, 58.65; H, 5.23; N, 17.01%. Calcd. for $\text{C}_{20}\text{H}_{19}\text{N}_5\text{O}_4$: C, 58.38; H, 5.15; N, 17.02%.

Benzoyl ester (XI) of the cyclonucleoside, IX. To a stirred and ice-cooled solution of IX (100 mg) in pyridine (5 ml) was added benzoyl chloride (200 mg). After 1 hr the solution was poured onto an ice-cooled solution of sodium bicarbonate and the product was extracted with chloroform. The solvent was evaporated and the residue was crystallized from carbon tetrachloride, yield 110 mg; mp 149~153°C; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 300 (11800) and 272 (15200); $\lambda_{\text{max}}^{\text{KBr}}$ 1710 cm^{-1} (ester-CO). Found: C, 59.04; H, 4.64; N, 12.80%. Calcd. for $\text{C}_{27}\text{H}_{25}\text{N}_5\text{O}_8$: C, 59.23; H, 4.60; N, 12.79%.

N⁵, 5'-Anhydro-5-formamido-4-(N-benzoylcarbamoyl)-1-(2,3-O-isopropylidene- β -D-ribofuranosyl)imidazole (XIII). A solution of IX (246 mg) dissolved in 70% aqueous acetic acid (50 ml) was heated on a water bath for 1 hr and was concentrated to dryness. The residue was applied to silicic acid chromatography with a mixture of benzene and ethyl acetate (1:1) and, then, with ethyl acetate. The fractions of the main product were collected, and the solvent was evaporated to give 138 mg of a syrup. For analysis it was fractionally precipitated from benzene and ligroin, $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 270 (10000) and 228 (18600); $[\alpha]_{\text{D}}^{24}$ -49.6 ($c=1.31$, CHCl_3); NMR (100 MHz, CDCl_3) δ : 1.28, 1.50 (two singlets, 6H, two isopropylidene methyls), 3.03 (q, 1H, $\text{H}_{\text{a}}-5'$, $J_{\text{gem}}=14$ Hz, $J_{4',5_{\text{a}}'}=1$ Hz), 4.74 (complex, 3H, $\text{H}-2'$, $\text{H}-3'$ and $\text{H}-4'$), 4.93 (q, 1H, $\text{H}_{\text{b}}-5'$, $J_{\text{gem}}=14$ Hz, $J_{4',5_{\text{b}}'}=2$ Hz), 5.93 (s, 1H, $\text{H}-1'$), 7.3~8.0 (complex, 6H, $\text{C}_6\text{H}_5\text{CO}-$ and $-\text{N}=\text{CH}-\text{N}<$) and 8.52 (s, 1H, $-\text{CHO}$); Mass m/e : 412 (M^+), 384 (M^+-CO), 280 ($\text{M}^+-\text{CO}-\text{C}_6\text{H}_5\text{CO}+\text{H}$), 121 ($\text{C}_6\text{H}_5\text{CO}-\text{NH}_2$). Found: C, 58.74; H, 5.02; N, 13.47%. Calcd. for $\text{C}_{20}\text{H}_{26}\text{N}_4\text{O}_6$: C, 58.25; H, 4.89; N, 13.58%.

N⁵, 5'-Anhydro-5-amino-4-carbamoyl-1-(2,3-O-isopropylidene- β -D-ribofuranosyl)imidazole (XIV). A solution of XIII (220 mg) dissolved in a mixture of methanol (5 ml) and 1 N NaOH (2.85 ml, four equivalents to XIII) was refluxed for 2 hr. The solution was concentrated and the product was extracted with chloroform. Evaporation of the solvent afforded 160 mg of a solid, which was shown to be homogeneous on TLC, and it was crystallized from benzene and carbon tetrachloride, double mp 103°C and 142~147°C; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 270 (9800) and 230 (6300); $[\alpha]_{\text{D}}^{24} +67.0$ ($c=1.10$, CHCl_3); NMR (100 MHz, CDCl_3) δ : 1.34, 1.54 (two singlets, 6H, two isopropylidene methyls), 3.2~3.4 (complex, 2H, $\text{H}-5'$), 4.59, 4.94 (a pair of doublets, 2H, $\text{H}-2'$ and $\text{H}-3'$), 4.66 (broad s, 1H, $\text{H}-4'$), 5.80 (s, 1H, $\text{H}-1'$), 6.38 (broad s, 1H, $-\text{NH}-\text{CH}_2-$, disappeared on addition of D_2O) and 7.27 (s, 1H, $-\text{N}=\text{CH}-\text{N}<$). Found: C, 51.87; H, 5.65; N, 19.70%. Calcd. for $\text{C}_{21}\text{H}_{16}\text{N}_4\text{O}_4$: C, 51.42; H, 5.75; N, 19.99%.

N², 5'-Anhydro-2-amino-3-(N-benzoylamidino)-1-(2,3-O-isopropylidene- β -D-ribofuranosyl)pyrrole (XVII). A

solution of XV⁶¹ (187 mg, 0.31 mm) dissolved in a mixture of methanol (30 ml) and 1 N NaOH (1 ml) was heated at 60~70°C for 1 hr. After the evaporation of methanol the product was extracted with chloroform. Evaporation of the chloroform afforded 40 mg of the residue, which was almost homogeneous on TLC. Crystallization from ethyl acetate and ligroin afforded an analytical sample, mp 220~223°C (dec); $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 355 (9800), 273 (18000) and 240 (15500); $[\alpha]_{\text{D}}^{24} +145$ ($c=1.65$, CHCl_3); NMR (100 MHz, CDCl_3) δ : 1.32, 1.54 (two singlets, 6H, two isopropylidene methyls), 3.36 (complex, 1H, $\text{H}-5'$), 4.59, 4.97 (a pair of doublets, $\text{H}-2'$ and $\text{H}-3'$, $J_{2',3'}=6$ Hz), 4.64 (broad, 1H, $\text{H}-4'$), 5.62 (s, 1H, $\text{H}-1'$), 6.14, 6.33 (a pair of doublets, $-\text{CH}=\text{CH}-\text{N}<$, $J_{7,8}=4$ Hz), 7.3~8.2 (complex, 5H, $\text{C}_6\text{H}_5\text{CO}-$) and 9.30 (broad s, 1H, $-\text{CH}_2-\text{NH}-$, disappeared on addition of D_2O); Mass m/e : 382.1664 (M^+ , $\text{C}_{20}\text{H}_{22}\text{N}_4\text{O}_4$ gives 382.1641), 261 ($\text{M}^+-\text{C}_6\text{H}_5\text{CONH}_2$), 241 (fragment XVIII). Found: C, 62.31; H, 5.69; N, 14.65%. Calcd. for $\text{C}_{20}\text{H}_{22}\text{N}_4\text{O}_4$: C, 62.81; H, 5.80; N, 14.65%.

3,5'-Anhydro-N⁶-benzoyl-2',3'-O-isopropylidene-uracil hydrate (XVI). A solution of XV (296 mg, 0.5 mm) dissolved in a mixture of methanol (30 ml) and 0.1 N NaOH (5 ml, 0.5 mm) was heated at 60~70°C for 1 hr. The methanol was evaporated, and the products were extracted with chloroform. Two compounds were isolated with silicic acid chromatography with a mixture of benzene and ethyl acetate (1:1), and the less polar one was identified as XVII, yield 19 mg. The other one, which was eluted from the column closely following XVII, was crystallized from ethyl acetate and was identified as XVI, yield 80 mg; mp 214~215°C; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 308 (12100), 272 (19500) and 248 (18600); $[\alpha]_{\text{D}}^{24} -204$ ($c=1.14$, DMSO); NMR (100 MHz, CDCl_3) δ : 1.32, 1.56 (two isopropylidene methyls), 3.21 (q, 1H, $\text{H}_{\text{a}}-5'$, $J_{\text{gem}}=15$ Hz, $J_{4',5_{\text{a}}'}=1$ Hz), 4.7~4.9 (complex, 3H, $\text{H}-2'$, $\text{H}-3'$ and $\text{H}-4'$), 5.04 (q, 1H, $\text{H}_{\text{b}}-5'$, $J_{\text{gem}}=15$ Hz, $J_{4',5_{\text{b}}'}=2$ Hz), 5.71 (s, 1H, $\text{H}-1'$), 6.42, 6.77 (a pair of doublet, 2H, $-\text{CH}=\text{CH}-\text{N}<$, $J_{7,8}=3$ Hz), 7.3~8.2 (complex, 5H, $\text{C}_6\text{H}_5\text{CO}-$) and 8.46 (s, 1H, $-\text{NH}-\text{HCOH}-\text{N}<$); Mass m/e : 410.1609 (M^+ , $\text{C}_{21}\text{H}_{22}\text{N}_4\text{O}_5$ gives 410.1590), 382 (M^+-CO), 392 ($\text{M}^+-\text{H}_2\text{O}$), 365 ($\text{M}^+-\text{CO}-\text{H}_2\text{O}$), 241 (fragment XIX). Found: C, 61.40; H, 5.40; N, 12.90%. Calcd. for $\text{C}_{21}\text{H}_{22}\text{N}_4\text{O}_5$: C, 61.45; H, 5.40; N, 13.05%.

N²,5'-Anhydro-2-formamido-3-(N-benzoylcarbamoyl)-1-(2,3-O-isopropylidene- β -D-ribofuranosyl)pyrrole (XX). A solution of XVI (200 mg) in 70% acetic acid was heated on a water bath for 4 hr, and was concentrated to dryness. The residue was extracted with chloroform and the organic layer was washed with water. The formation of several products was shown by TLC and the main one was isolated with silicic acid chro-

matography with a mixture of benzene and ethyl acetate (1:1), yield 50 mg; mp 117~121°C; $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (ϵ): 280 (shoulder, 7000) and 243 (23000); $[\alpha]_{\text{D}}^{24} -72.3$ ($c=1.02$, CHCl_3); NMR (100 MHz, CDCl_3) δ : 1.29, 1.52 (two singlets, 6H, two isopropylidene methyls), 3.01 (q, 1H, H_a-5' , $J_{\text{gem}}=15$ Hz, $J_{4',5_a'}=2$ Hz), 4.6~4.8 (broad, 3H, $\text{H}-2'$, $\text{H}-3'$ and $\text{H}-4'$), 4.85 (q, 1H, H_b-5' , $J_{\text{gem}}=15$ Hz, $J_{4',5_b'}=2$ Hz), 4.6~4.8 (broad, 3H, $\text{H}-2'$, $\text{H}-3'$ and $\text{H}-4'$), 4.85 (q, 1H, H_b-5' , $J_{\text{gem}}=15$ Hz, $J_{4',5_b'}=3$ Hz), 5.67 (s, 1H, $\text{H}-1'$), 6.42, 6.72 (a pair of doublet, $-\text{CH}=\text{CH}-\text{N}<$, $J_{7,8}=4$ Hz), 7.4~7.9 (complex, 5H, $\text{C}_6\text{H}_5\text{CO}-$) and 8.42 (s, 1H, $>\text{N}-\text{CHO}$); Mass m/e : 411.1401 (M^+ , $\text{C}_{21}\text{H}_{21}\text{N}_3\text{O}_6$ gives 411.1430), 383 (M^+-CO).

The same compound had already been obtained as one of the products in the reaction of XV with sodium iodide.⁶⁾

REFERENCES

- 1) K. Anzai, G. Nakamura and S. Suzuki, *Antibiotics*, **A 10**, 201 (1957).
- 2) S. Suzuki and S. Marumo, *ibid.*, **A 13**, 360 (1960).
- 3) Y. Mizuno, M. Ikehara, K. A. Watanabe, S. Suzuki and T. Itoh, *J. Org. Chem.*, **28**, 3329 (1963).
- 4) R. Kuhn and W. Jahn, *Ber.*, **98**, 1699 (1965).
- 5) W. Jahn, *ibid.*, **98**, 1706 (1965).
- 6) K. Anzai and M. Matsui, *Bull. Chem. Soc. Japan*, **46**, 618 (1973).
- 7) W. Anderson, D. H. Hayes, A. M. Michelson and A. R. Todd, *J. Chem. Soc.*, **1954**, 1882.
- 8) V. M. Clark, A. R. Rodd and J. Zussman, *ibid.*, **1951**, 2952.
- 9) B. R. Baker and J. P. Joseph, *J. Am. Chem. Soc.*, **77**, 15 (1955).