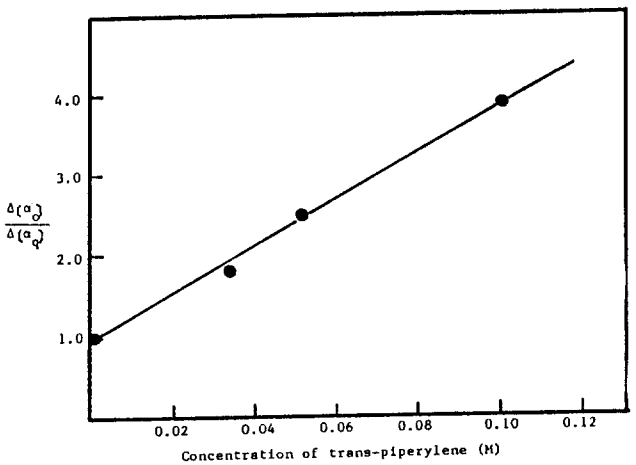
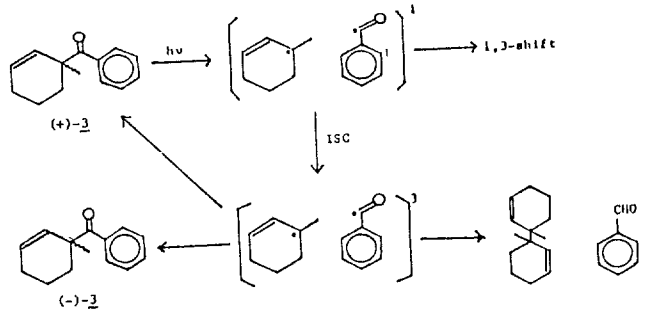


Figure 1. Stern-volmer quenching of the photo-racemization of (–)-ketone **3**.

Based upon these facts, the racemization mechanism was suggested as follows:



The mechamism involves α-cleavage to yield alkyl and benzoyl radical, which recombine to afford racemization.

Since the efficient racemization was quenched and the fluorescence emission was not detected, an efficient intersystem crossing may prevent producing 1,3-shift product, which generally comes from singlet state. Ketone **3** is one of a few[8-11] ketones which intersystem cross under the direct irradiation condition. The direct vs. sensitized triplet state of ketone **3** including racemization, 1,3-shift and the oxa-di-π-methane (ODPM) rearrangement products are under investigation.

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6. A solution of 329 mg (1.65 mmol) of (+)-**3** in 15 m*l* of dried ether was degassed with purified nitrogen. Irradiation was carried out with 4 RPR-3500 Å lamps. Light output was minitored by potassium ferrioxalate actinometry according to the method of Hatchard and Parker, *Proc. Roy. Soc., Ser. A.* **235**, 518 (1956).
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O-Debenzoylation and Methoxylation of Some Tribenzoylated Pyridazine Nucleosides

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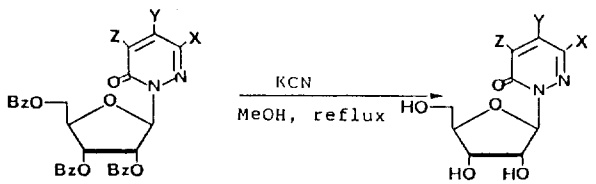
In connection with our research for the synthesis of some biologically active pyridazine nucleosides, we have attempted the synthesis of some cyanopyridazine nucleosides from mono- or dichloropyridazine nucleosodes with the fully benzoylated sugar moiety and KCN in methanol solvent. We have, however, obtained the corresponding mono- and dimethoxypyridazine nucleosides with the fully debenzoylated sugar moiety instead of cyanopyridazine nucleosides containing the protected sugar moiety. On the other hand, mono- or dicyanopyridazine nucleosides were synthesized from CuCN-DMSO system.[1]

This preliminary result is interesting in nucleic acid chemistry. The deprotection of benzoyl or acyl groups on 2′, 3′ and 5′-positions of sugar moiety is one of the most important procedure in the field of sugar, nucleoside and nucleotide chemistry. In general, acyl groups of protected esters have

been removed by treatment with ammonium hydroxide,[2] hydrazine hydrate,[3-5] aluminum oxide,[6] alcohol,[7] alkoxides.[8-10] However, when strong bases have been used, O-acyl groups on the ribofuranosyl ring sometimes migrate to another position.[11-13] In this point of view, the development of novel method for O-debenzoylation of the fully acylated sugar under mild condition is necessary in nucleic acid chemistry.

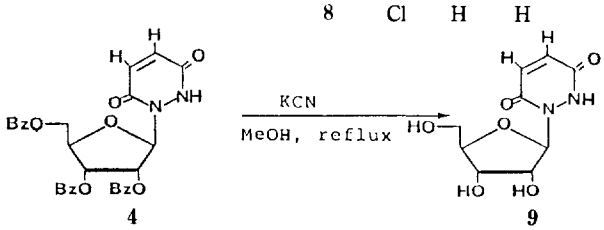
In this paper, we have reported the results on the debenzoylation of multisubstituted pyridazine nucleosides with the fully benzoylated sugar moiety at 2′, 3′, and 5′-positions in the presences of KCN in methanol solvent at reflux temperature.

Reaction of 4,5-dichloro-3-nitro-1-(2′,3′,5′-tri-O-benzoyl-1-β-D-ribofuranosyl)pyridazin-6-one(**1**) with KCN in methanol for 5 hours at reflux gave the compound **5** and **6** in 10% and 17% yield, respectively. Reaction of 4,5-dichloro-1-(2′,3′,5′-tri-O-benzoyl-β-D-ribofuranosyl)- pyridazin-6-one (**2**) with KCN in methanol for 3.5 hours at reflux also gave the compound **7** in 70% yield, whereas reaction of 3-chloro-1-(2′,3′,5′-tri-O-benzoyl-β-D-ribofuranosyl) pyridazin-6-one (**3**) and 1-(2′,3′,5′-tri-O-benzoyl-β-D-ribofuranosyl)pyridazin 3,6-dione (**4**) with KCN in methanol gave the compound **8** (57%) and **9** (86%), respectively. Townsend *et al.*[8-10] also prepared the compound **5**, **6**, **7** and **8** from compound **1**, **2**, and **3** using sodium methoxide in methanol. Few procedures for the transesterification,[14] deacylation[16-18] and deesterification[19] using KCN in an alcohol have been reported. It was found that the reaction of methyl esters of cyclohexenone derivatives with KCN-EtOH(excess) gave the corresponding ethyl esters, through an acyl cyanide intermediate by Brich *et al.*[14] It has also been reported that the reactivity toward base of benzoyl groups on the benzoylated sugar in nucleoside, in general increases in order of 2′>3′>5′-position.[4] Also, our research of the reactions monitored by TLC revealed that the first attack of the nucleophile take place at 2′-position to form 2′-hydroxy compound and then 3′ and 5′-position benzoyl groups are deprotected. This procedure may be useful for the benzoylation of benzoylated sugars. This finding is very interesting in the methoxylation of multisubstituted heterocyclic compounds with sensitive functional groups under mild condition. Additional reactions of this procedure are currently under investigation in our laboratory.



1-3 **5-8**

	X	Y	Z		Z	Y	Z
1	NO_2	Cl	Cl	5	OCH_3	OCH_3	Cl
2	H	Cl	Cl	6	OCH_3	Cl	OCH_3
3	Cl	H	H	7	H	OCH_3	Cl
				8	Cl	H	H



4 **9**

Synthesis of 4-chloro-3,5-dimethoxy-1-β-D-Ribofuransyl Pyridazin-6-one(5) and 5-Chloro-3,4-dimethoxy-1-β-D-ribofuranosyl Pyridazin-6-one(6). A mixture of fully O-benzoylated nucleoside **1**(2g, 3.1mmol), KCN(0.59g, 9.2mmol) and methanol(30 m*l*) was refluxed with stirring for 5 hours. The resulting mixture was cooled ambient temperature and treated with 4g of Amberlite IRC-50 resin(H^+-form) for 24 hours to remove the residue KCN. The resulting solution was filtered through silica gel column (3 × 10 cm) and the eluant was coevaporated with 4g of silica gel and the silica gel was applied to the top of open bed column(2.5 × 30cm). The column was eluted with 600 m*l* of chloroform/methanol (8:2, v/v). After the first 400 m*l* of solvent was discarded, 8 m*l* fraction was collected. Nucleoside product was detected in fractions 61-70 and fractions 76-80. Fractions 61-70 were combined and evaporated under reduced pressure to give **5** as a white powder. Yield 9 mg(10.2%); mp; 108-110 °C (lit.[10] 110-111 °C); IR(KBr) 3400, 2940, 1640, 1600 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 6.19(d, $H_{1'}$, J = 3Hz), 4.13(s, OCH_3), 3.78(s, OCH_3), 4.52-5.22(m, $OH_{2'}$ + $OH_{3'}$ + $OH_{5'}$ = 3OH, D_2O exch.) 4.10-3.81(m, $H_{2'}$ + $H_{3'}$ + $H_{4'}$ + $H_{5'}$ = 5H). Fractions 76-82 were combined and evaporated under reduced pressure to give **6** as a white powder. Yield 163mg (17%); mp 168-173 °C (lit.[10] 169-173 °C); IR(KBr) 3400, 2940, 1640, 1600 cm^{-1}; ^{1}H-NMR(DMSO-d_6) δ 6.20(d, $H_{1'}$, J = 3Hz), 4.60(s, OCH_3), 4.5-5.2(m, $OH_{2'}$ + $OH_{3'}$ + $OH_{5'}$ = 3OH, D_2O exch.), 4.12-3.81 (m, $H_{2'}$ + $H_{3'}$ + $H_{4'}$ + $H_{5'}$ = 5H).

Synthesis of 5-Chloro-4-methoxy-1-β-D-ribofuranosyl Pyridazin-6-one(7). Nucleoside **2**(1g, 1.6mmol), KCN (0.115g, 1.76mmol) and methanol (30 m*l*) was refluxed with stirring for 3.5 hours. The reaction mixture was cooled to ambient temperature and added 2g of Amberlite IRC-50 resin (H^+-form) and stirred for additional 4 hours. The reaction mixture was filtered and coevaporated with 3g of silica gel and applied to the top of open bed column. The columm was eluted with 400 m*l* of chloroform/methanol (8:2, v/v). After the first 200 m*l* of eluant was discarded, 8 m*l* fraction was then collected. The fractions containing the nucleoside were combined and evaporated under reduced pressure to give **7** as a white powder. Yield 336 mg(70%); mp 158-160 °C (lit.[8,9] 161-163 °C); IR(KBr) 3400, 2970, 1650, 1600 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 8.38(s, H_3), 6.25(d, $H_{1'}$, J = 3.1Hz), 5.25(m, $OH_{2'}$, D_2O exch.), 4.98(m, $OH_{3'}$, D_2O exch.), 4.51(m, $OH_{5'}$, D_2O exch.), 4.18(s, OCH_3), 4.25-3.75(m, $H_{2'}$ + $H_{3'}$ + $H_{4'}$ + $H_{5'}$ + 5H).

Synthesis of 3-Chloro-1-β-D-ribofuranosyl Pyridazin-6-one(8). Nucleoside **3**[9](1g, 1.7mmol), KCN(0.67g 10mmol) and methanol (50 m*l*) was refluxed with stirring for 6 hours. The reaction mixture was cooled to ambient temperature and added 4g of Amberlite IRC-50 resin (H^+-form) and stirred for an additional 12 hours. The reaction mixture was filtered and coevaporated with 3g of silica gel and applied to the top of open bed column. The column was eluted with 400 m*l* of chloroform/methanol(8:2, v/v). After the first 200 m*l* of eluant was discarded, the eluant was collected in 8 m*l* fractions. The fractions containing nucleoside product were combined and evaporated under reduced pressure to give 8 as a pale yellow powder. Yield 300 mg(57%); mp 147-150 °C (lit.[8,9] 151-152 °C); IR(KBr) 3400, 2950, 1680, 1650 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 7.55-7.70(d, H_4, J = 9Hz), 7.01-6.94(d, $H_{5'}$, J = 8Hz), 6.02-6.03(d, $H_{1'}$, J = 3.2Hz), 5.31-5.20(d, J = 4Hz, D_2O exch), 5.11-4.99(d, $OH_{3'}$, J = 3.2Hz,

D_2O exch.), 4.75-4.51(m, $OH_{5'}$, D_2O exch.) 4.41-3.82(m, $H_{2'} + H_{3'} + H_{4'} + H_{5'} = 5H$).

Synthesis of 1-β-D-ribofuranosyl Pyridazin-3,6-dione(9). Nucleoside **4**[20](1g, 1.8mmol), KCN(0.67g, 10mmol) and methanol (50 m*l*) was refluxed with stirring for 6 hours. After cooling to ambient temperature, to the reaction mixture was added 4g of Amberlite IRC-50 resin (H^+-form) and stirred for additional 12 hours. The reaction mixture was filtered and coevaporated with 3g of silica gel under reduced pressure and applied to the top of open bed column (2.5 × 30 cm). The column was eluted with 600 m*l* of chloroform/methanol (8:2, v/v). After the first 300 m*l* of eluant was discarded, the eluant was collected in 8 m*l* fractions. The fractions containing nucleoside product were combined and evaporated under reduced pressure to give **9** as a white powder. Yield 370mg (86%); mp 300 °C (dec.); IR(KBr) 3400, 2940, 1660, 1640 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 7.56-7.41(d, H_5, J = 8Hz), 7.00-6.91(d, H_5, J = 8.5Hz), 6.00-5.97(d, $H_{1'}$, J = 3Hz), 5.32-5.22(d, $OH_{2'}$, J = 5Hz, D_2O exch), 5.00-4.97(d, $OH_{3'}$, J=4.7Hz, D_2O exch.), 4.61-4.42(m, $OH_{5'}$, D_2O exch.), 4.21-3.61(m, $H_{2'} + H_{3'} + H_{4'} + H_{5'} = 5H$).

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20. Nucleoside **4** was synthesized by using the method of Townsend *et al.*[8-10]; Maleic hydrazide 2g (17.84 mmol) was silylated by heating at reflux for 2 hours in hexamethyldisilazane (30 m*l*) with 0.6g (4.5 mmol) of ammonium sulfate. The excess hexamethyldisilazane was removed by distillation under reduced pressure and the remaining solid was used without further purification. The silylated heterocycle and 1-O-acetyl-2,3,5-tri-O-benzoyl-1-β-D-ribofuranose (7.5g, 17.5mmol) were dissolved in dry dichloroethane (50 m*l*) and the solution was cooled to 0 °C. Stannic chloride (3.9 m*l*, 14.04 mmol) was added and the solution heated at reflux temperature for 0.5 hours. The reaction mixture was cooled to 0 °C and ethanol (50 m*l*) and sodium bicarbonate (13g) were added, and the mixture was stirred for 5 hours. The gelatinous mass was evaporated to dryness under reduced pressure. The remaining solid mass was extracted with boiling chloroform (3 × 300 m*l*). The chloroform extracts were combined and passed through silica gel column (3 × 35 cm). The eluant was evaporated under reduced pressure to give a white powder. The white powder was crystallized from ethyl alcohol. Yield 8.1g (85%); mp 199-202 °C; IR(KBr) 3450, 3070, 2950, 1750, 1690, 1580 cm^{-1}; ^{1}H-NMR(DMSO-d_6) δ 11.6(s, NH, D_2O exch.), 8.01-7.3(Bz-H), 7.28(d, H_4, J = 9Hz), 7.00(d, H_5, J = 8.7Hz), 6.7(d, $H_{2'}$, J = 2Hz), 6.3-5.9(m, $H_{2'} + H_{3'}$), 4.5-4.05(m, $H_{4'} + H_5$).