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Preliminary communication

Novel activating and *O*→*N* glycosyl migrating agents in the condensation reactions of 2(1*H*)-pyridone or 4-methoxy-2(1*H*)-pyrimidinones with a 1-*O*-phenoxycarbonyl sugar derivative*

MASAHIDE YAMADA, SHIGERU INABA, TERUO YOSHINO, and YOSHIHARU ISHIDO

Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, O okayama, Meguro-ku, Tokyo (Japan)

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In a previous communication*, a new procedure for the synthesis of glycosyl compounds that uses a 1-*O*-phenoxycarbonyl sugar derivative was described, 2(1*H*)-pyridone (**1**) and 4-methoxy-2(1*H*)-pyrimidinone (**2**) selectively afforded the corresponding *O*-glycosyl compounds, although their yields barely exceeded 30% With the immediate goal of improving yields in this novel reaction, the authors have made a study of various activating agents that have been found useful in the condensation of purine derivatives with fully acylated sugars[1]

To a homogeneous, prefused mixture of **1** (0.3 g, 3 3 mmoles) and *p*-toluenesulfonamide (**3**) (0 6 g, 3 3 mmoles) at 135–140° was added 2,3,4,6-tetra-*O*-acetyl-1-*O*-(phenoxycarbonyl)-β-D-glucopyranose (**4**) (1 5 g, 3 3 mmoles), and the mixture was stirred for 1 h at 135–140°/20 torr to remove the phenol liberated The remaining phenol and unchanged **1** and **3** were removed by washing with 1 M aqueous sodium hydroxide, and two recrystallizations of the residue from ethanol afforded 2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyloxy)pyridine* (**5**) (1 1 g, 78 5% yield), the yield of **5** was thus greatly improved

On increasing the molar ratio of **3** to the other reagents as shown in Table I, we confirmed that 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2(1*H*)-pyridone* (**6**) is concomitantly produced, and the application of five molar equivalents of **3** resulted in the preponderant formation of **6** (1 0 g, 71 4% yield) Compound **2** and 4-methoxy-5-methyl-2(1*H*)-pyrimidinone similarly afforded the acetates of the corresponding *N*-glycosyl compounds in 45* and 57% yields, respectively The latter compound had m p 132–133°, $[\alpha]_D^{22}$ −14 2° (*c* 1 0, chloroform), and λ_{max}^{EtOH} 283 nm (ϵ_{mM} 6 95). Elemental analytical data were consistent with those calculated for the expected structure These results suggested

* Synthetic Studies by the Use of Carbonates. Part V. For Part IV, see S. Inaba, Y Yamada, T. Yoshino, and Y Ishido, *J Amer Chem. Soc* , 95 (1973) 2063.

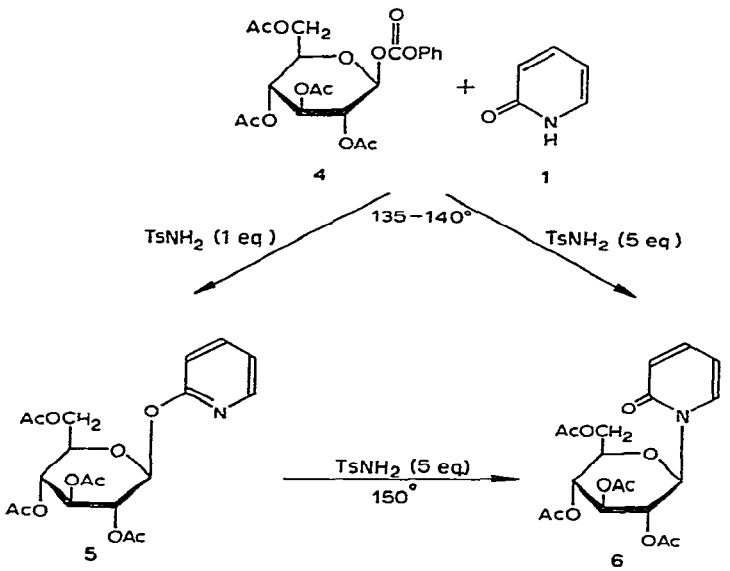

TABLE I

CONDENSATION OF 2(1*H*)-PYRIDONE (1) WITH 2,3,4,6-TETRA-*O*-ACETYL-1-*O*-(PHENOXYCARBONYL)-β-D-GLUCOPYRANOSE (4) IN THE PRESENCE OF *p*-TOLUENESULFONAMIDE (3) [a]

Molar ratios of reagents			*Relative percentages of products* [b]	
1	4	3	5	6
1	1	1	100 (78 5% [c])	–
1	1	2	100	trace [d]
1	1	3	54 5	45 5
1	1	4	33 3	66 6
1	1	5	–	100 (71 4% [c])
1	1	5 [e]	37 5	62 5

[a] All reactions were conducted with 3 3 mmoles of 1 by fusing each mixture for 1 h at 135–140° *in vacuo* [b] These percentages were calculated from the integration curve of each n m r spectrum [c] The yields are those of the corresponding glycosyl compounds [d] This was detected by t l c [e] This reaction was performed at atmospheric pressure

that migration of the glycosyl group of 5 to give 6 might have been induced by 3 in the course of the reaction, this hypothesis was verified when it was found that fusion of 5 with five molar equivalents of 3 under similar reaction-conditions, followed by direct crystallization from ethanol, afforded 6 in a yield of 78% It is significant that the *O*→*N* glycosyl migration can be induced by such organic agents as 3 as effectively as with mercuric bromide[2], and that synthesis of either an *O*- or an *N*-glycosyl compound is now

possible at will, merely by appropriately adjusting the reaction conditions as described

This discovery led us to test the potential application of other activating agents[1] to such a reaction system *N*-Methyl- (**7**), *N,N*-dimethyl- (**8**), and *N*-acetyl-*p*-toluenesulfonamide (**9**), benzenesulfonamide (**10**); *p*-chloro- (**11**) and *p*-nitro-benzenesulfonamide (**12**), benzamide (**13**), *o*- (**14**), *m*- (**15**), and *p*-nitrophenol (**16**), phenol (**17**), and succinimide (**18**) were examined for their possible catalytic effect in the *O*→*N* glycosyl migration under the same reaction conditions The relative ratios of **5** and **6** in each of the product mixtures were calculated from the integration curve of their respective n m r spectra,because a one-proton signal for the pyridine ring of **5** is observed at δ 8 20 p p m (chloroform-*d*, tetramethylsilane) apart from the other aromatic-ring protons The relative proportions of **5** and **6** in the respective products can thus be calculated from the integration curve of each spectrum The agents **10**, **11**, **12**, and **15** were found to isomerize **5** into **6** entirely, **9** and **16** were also effective, although they concomitantly afforded *N*-acetyl-*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*p*-toluenesulfonamide** (25%) and *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside*** (33%), respectively, catalysts **7** and **13** converted **5** into **6** to the extent of 70 and 16%, respectively. Compounds **8**, **14**, **17**, and **18** showed no catalytic effect at all However, compound **14** was found to be synthetically advantageous, as it gave solely **5** (in 84 5% yield) when applied to the condensation reaction of **1** with **4**

REFERENCES

1 M. Sekiya, T Yoshino, and Y Ishido, *Bull Chem. Soc Jap*, 46 (1973) 556
2 J. A. Elvidge, G T Rogers, and T L. V. Ulbricht, *J Heterocycl Chem.*, 8 (1971) 1039, H Pischel, A. Holý, and G Wagner, *Collect Czech Chem. Commun*, 37 (1972) 3475

** This product was identified by n m.r spectroscopy in comparison with an authentic specimen {m.p 75–76°, $[\alpha]_D^{22}$ −9° (*c* 1 0, chloroform)} prepared by another procedure. Preparation of the specimen will be reported elsewhere, together with that of the other related compounds

*** This product was identified by comparison with an authentic specimen [E M. Montgomery, N K. Richtmyer, and C. S Hudson, *J Amer Chem. Soc*, 64 (1942) 690] by n m.r spectroscopy