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Synthesis of O-Glycosides of Heteroatom Aroyl-Substituted Heterocyclic Ketene Aminals

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Abstract: Heteroatom aroyl-substituted heterocyclic ketene aminals **1** reacted with 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide **2** under the catalysis of $Hg(CN)_2$ or CaH_2 to give *E*- or *Z*- O-glycosides of heterocyclic ketene aminals **3** or **4** in moderate yields.

Keywords: Synthesis, heterocyclic ketene aminals, O-glycosides.

As we know, carbohydrates play an important role in nature, especially as recognition determinant in host-pathogen interactions or in cell-cell interactions. Therefore, stereo-controlled glucosylation has become one of the important topics in organic synthesis [1,2].

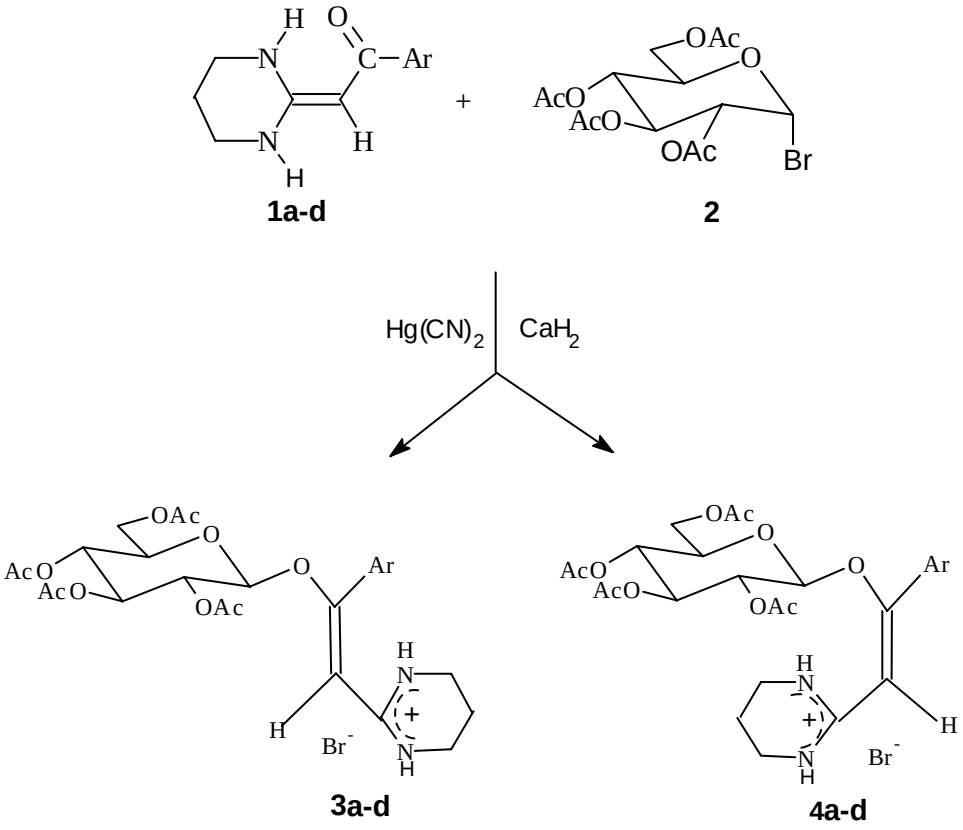
Heterocyclic ketene aminals are important intermediates for the synthesis of a wide variety of new heterocycles and fused heterocycles, some of which have high biological activity[3]. It has been reported that benzoyl-substituted heterocyclic ketene aminals can react with **2** using mercuric cyanide as catalyst to give E-configuration O-glycosided heterocyclic ketene aminals[4]; *E*- or *Z*-configuration O-galactosides of heterocyclic ketene aminals were yielded when heterocyclic ketene aminals reacted with 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide under the catalysis of $Hg(CN)_2$ or CaH_2, respectively[5]. Here, we wish to report the reaction of heteroatom aroyl-substituted heterocyclic ketene aminals **1** with **2** under the catalysis of $Hg(CN)_2$ or CaH_2.

Heterocyclic ketene aminals **1** were prepared by the reaction of 1,3-diaminopropane and α-oxo ketene dithiacetals[6]. **1** reacted with 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide **2** in the presence of $Hg(CN)_2$ to give the products **3** in moderate yields. However, when **1** and **2** reacted under the catalysis of CaH_2, **4** were yielded. The reaction conditions, yields and melting points are listed in **Table 1**.

The structures of **3** and **4** were established by MS, IR, NMR and elemental analysis[7]. In the ^{1}H-NMR of **3** and **4**, the signals of two nitrogen protons (8.57-9.40 ppm) and one ethylenic proton (6.21-6.80 ppm) and the appearance of a new carbon signal (155.22-161.38 ppm) instead of a carbonyl carbon signal (*ca*. 180 ppm) indicate that O-glycosides were formed. The β linkage of the acetyl-protected glucopyranosyl group to heterocyclic ketene aminals was confirmed by the H_1-H_2 coupling constants (7.56-8.05 Hz) of the glucopyranosyl ring[8]. The Z-configuration of **4** was proved by the shift to

lower field of the ethylenic proton compared to the E-configuration of **3** due to the deshielding effect of the aryl goup[5].

Scheme 1.



1a-d **2** **3a-d** **4a-d**

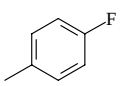
1,3,4	a	b	c	d
Ar				

Table 1. Reaction conditions of **1** with **2**, yields and melting points of compounds **3**-**4**

Reaction condition			Product	Yield[a] (%)	Melting point
Method	Temp. (°C)	Time (d)			(°C)
A	30	1	**3a**	77	72-74
A	30	1	**3b**	69	88-90
A	30	1	**3c**	68	66-68
A	30	1	**3d**	82	69-71
B	30	5	**4a**	62	76-78
B	30	14	**4b**	42	81-83
B	30	4	**4c**	48	79-81
B	30	2	**4d**	75	73-75

[a] Isolated yield

A: $Hg(CN)_2$ as catalyst in CH_3CN

B: CaH_2 as catalyst in CH_3CN

Acknowledgments

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7. Spectroscopic data of some selected compounds:
   3a IR: 3390, 1750, 1660, 1620; ^{1}H-NMR ($CDCl_3$): 9.02 (s, 2H, NH), 7.58-7.63 (m, 1H, Ar-H), 7.07-7.13 (m, 1H, Ar-H), 6.72 (s, 1H, C=CH), 6.53-6.59 (m, 1H, Ar-H), 5.50 (d, 1H, Glu-H_1, $J_{H1,\ H2}$ = 7.82 Hz), 5.36 (t, 1H, Glu-H_2), 5.04-5.24 (m, 2H, Glu-H_3, H_4), 3.92-4.32 (m, 2H, Glu-H_6), 3.65-3.78 (m, 1H, Glu-H_5), 3.60 (t, 4H, N-CH_2), 2.20 (s, 3H, $COCH_3$), 2.10, (s, 9H, $COCH_3$), 2.02 (quin, 2H, C-CH_2-C); ^{13}C-NMR ($CDCl_3$): 170.41, 170.05, 169.48, 169.15, 155.22, 150.81, 145.46, 145.26, 115.04, 112.34, 99.37, 98.50, 72.63, 71.31, 71.04, 67.65, 61.05, 38.74, 20.61, 20.45, 20.24, 20.23, 17.83; FAB-MS: 523 $(M\text{-}Br)^+$.
   Anal. calcd. for $C_{24}H_{31}BrN_2O_{11}$: C, 47.77; H, 5.18; N, 4.64. Found: C, 47.52; H, 5.20; N, 4.54.
   4a IR: 3410, 1750, 1660, 1622; ^{1}H-NMR ($CDCl_3$): 9.25 (s, 2H, NH), 7.58-7.60 (m, 1H, Ar-H), 7.05-7.10 (m, 1H, Ar-H), 6.80 (s, 1H, C=CH), 6.53-6.58 (m, 1H, Ar-H), 5.50 (d, 1H, Glu-H_1, $J_{H1,\ H2}$ = 8.05 Hz), 5.35 (t, 1H, Glu-H_2), 5.02-5.22 (m, 2H, Glu-H_3, H_4), 3.90-4.30 (m, 2H, Glu-H_6), 3.63-3.75 (m, 1H, Glu-H_5), 3.57 (t, 4H, N-CH_2), 2.20, 2.02, 2.01, 2.00 (s, 12H, $COCH_3$), 1.95-2.05 (m, 2H, C-CH_2-C); ^{13}C-NMR ($CDCl_3$): 170.48, 170.03, 169.25, 169.15, 155.28, 150.77, 145.45, 145.30, 114.94, 112.33, 99.25, 98.46, 72.70, 71.26, 71.08, 67.70, 61.08, 38.62, 20.60, 20.43, 20.26, 20.25, 17.86; FAB-MS: 523 $(M\text{-}Br)^+$.
   Anal. calcd. for $C_{24}H_{31}BrN_2O_{11}$: C, 47.77; H, 5.18; N, 4.64. Found: C, 47.19; H, 5.29; N, 4.51.

3c IR: 3390, 1750, 1665, 1625; ^{1}H-NMR ($CDCl_3$): 9.17 (s, 2H, NH), 8.60 (d, 1H, Ar-H), 7.84-8.00 (m, 2H, Ar-H), 7.35-7.43 (m, 2H, Ar-H), 6.74 (s, 1H, C=CH), 6.04 (d, 1H, Glu-H_1, $J_{H1,H2}$ = 8.31 Hz), 5.33 (t, 1H, Glu-H_2), 4.95-5.15 (m, 2H, Glu-H_3, H_4), 3.72-4.04 (m, 2H, Glu-H_6), 3.62 (t, 4H, N-CH_2), 3.26-3.35 (m, 1H, Glu-H_5), 2.20, 2.08, 2.02, 1.98 (s, 12H, $COCH_3$), 2.01-2.10 (m, 2H, C-CH_2-C); ^{13}C-NMR ($CDCl_3$): 171.66, 170.16, 169.65, 169.31, 159.13, 155.63, 150.48, 148.34, 138.05, 124.97, 124.75, 102.34, 96.64, 72.41, 71.51, 71.30, 68.05, 61.21, 38.94, 20.99, 20.62, 20.43, 20.42, 18.03; FAB-MS: 534 $(M\text{-}Br)^+$.

Anal. calcd. for $C_{25}H_{32}BrN_3O_{10}$: C, 48.87; H, 5.25; N, 6.84. Found: C, 48.49; H, 5.52; N, 6.57.

4c IR: 3390, 1750, 1665, 1625; ^{1}H-NMR ($CDCl_3$): 9.39 (s, 2H, NH), 8.52 (d, 1H, Ar-H), 7.75-7.80 (m, 2H, Ar-H), 7.28-7.36 (m, 2H, Ar-H), 6.80 (s, 1H, C=CH), 6.00 (d, 1H, Glu-H_1, $J_{H1, H2}$ = 8.20 Hz), 5.25 (t, 1H, Glu-H_2), 4.85-5.04 (m, 2H, Glu-H_3, H_4), 3.60-3.95 (m, 2H, Glu-H_6), 3.54 (t, 4H, N-CH_2), 3.17-3.27 (m, 1H, Glu-H_5), 2.04, 1.98, 1.92, 1.85 (s, 12H, $COCH_3$), 1.90-2.00 (m, 2H, C-CH_2-C); ^{13}C-NMR ($CDCl_3$): 171.61, 169.99, 169.52, 169.20, 158.97, 155.56, 150.44, 148.32, 137.83, 124.88, 124.29, 102.04, 95.52, 72.32, 71.47, 71.15, 67.93, 61.12, 38.66, 20.88, 20.46, 20.33, 20.30, 17.94. FAB-MS: 534 $(M\text{-}Br)^+$.

Anal. calcd. for $C_{25}H_{32}BrN_3O_{10}$: C, 48.87; H, 5.25; N, 6.84. Found: C, 48.40; H, 5.15; N, 7.32.

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