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[2+2]Cycloaddition of Trichloroacetyl Isocyanate to Furanoid Glycals

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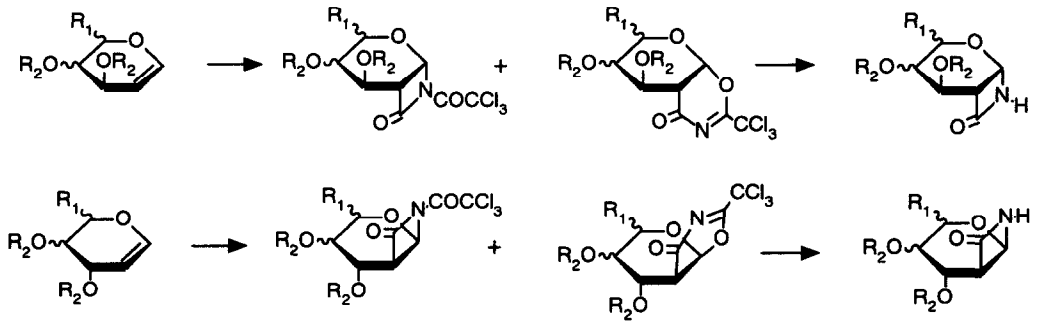
Abstract. Reaction between furanoid glycals **1-3** and trichloroacetyl isocyanate yielded a mixture of [2+2] and [4+2]cycloadducts. The isocyanate entered a glycal molecule exclusively *anti* with respect to the substituent at the C-3 carbon atom. Deprotection of the nitrogen atom in the [2+2]cycloadduct produced stable bicyclic ß-lactams **10-12**.

Recently we have described of [2+2]cycloaddition of isocyanates to pyranoid glycals.[1,2] Trichloroacetyl isocyanate and glycals having nonpolar protecting groups have been found to be the most suitable substrates for cycloaddition, reacting readily at room temperature and atmospheric pressure, providing relatively stable cycloadducts, and offering an isocyanate-activating substituent readily removable from the cycloadducts under mild conditions. The isocyanate has been found to enter a glycal molecule *anti* with respect to the substituent at the C-3 carbon atom.[1,2] (Scheme 1) Owing to that stereospecificity, cycloaddition offers a stereocontrolled entry to 1-oxabicyclic β-lactams.[3]

Scheme 1



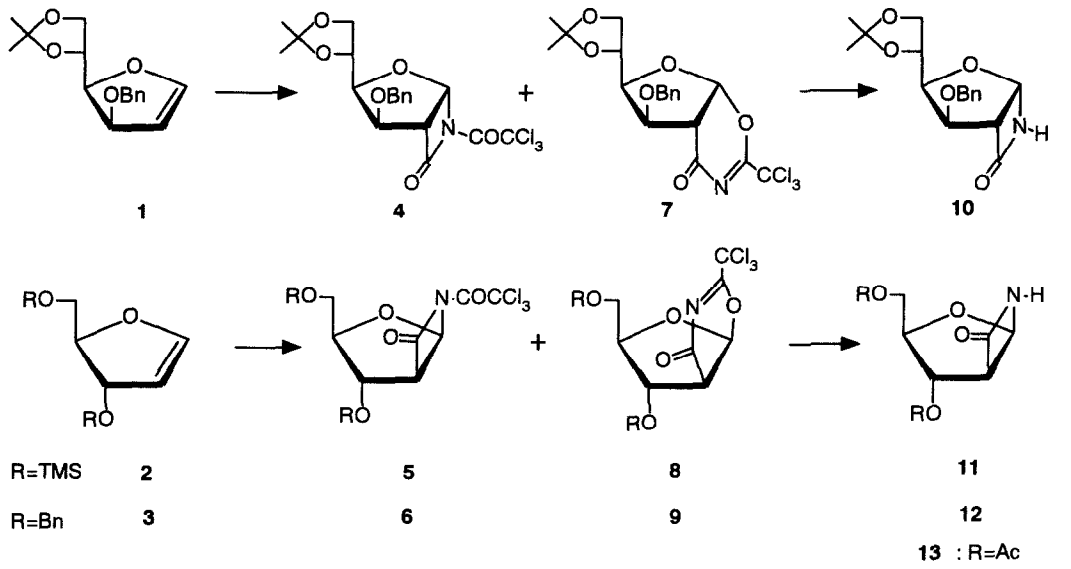
[2+2]Cycloaddition of trichloroacetyl isocyanate to furanoid glycals would be a logical supplement to our previous investigations.[1,2] Bicyclic ß-lactams having a four-membered ring fused to the furanoid ring have been obtained in the past by a two-step contraction of the pyranoid ring.[4,5]

In this work, as substrates we selected glycal **1** readily available from 2,3:5,6-di-*O*-isopropylidene-D-mannose[6] and glycals **2** and **3**[7] of an alternative configuration at the C-3 carbon atom (Scheme 2).

Cycloaddition was performed at room temperature in acetonitrile (0.5 mmol of the glycal in 1ml) using 1.5 molar equivalent of trichloroacetyl isocyanate. Reaction was completed within 1-3 h (pilot experiments in a NMR-test tube)[8] affording in each case a mixture of [2+2] **4-6** and [4+2]cycloadducts **7-9** in a 1:1 ratio. Upon prolongation of the reaction time, [4+2] cycloadducts **7-9** became the main components. After finding from the NMR experiment[8] the optimal time for ß-lactam formation (**4-6**), the reaction mixture was cooled to -5 °C and treated with benzylamine (2 molar equiv.). The stable bicyclic ß-lactams **10-12**[9] were isolated by chromatography in 18%, 30%, and 21% yields respectively. The α-D-gluco configuration for **10** and ß-D-arabino configuration for **11** and **12** were assigned consistently with the small $J_{2,3}$ coupling constant (below resolution), thus proving that the cycloaddition proceeded exclusively *anti* to the 3-*O*-benzyl or 3-*O*-silyl group

present in the substrate (**1-3**), and that the configuration at the C-4 carbon atom did not affect that of the adduct. The configuration of compound **13** was also proved by X-ray crystallography.[10]

Scheme 2



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References and notes

1. Chmielewski, M.; Kałuża, Z.; Grodner, J.; Urbański, R. *ACS Symposium series*; Giuliano, R. M., Ed.; **1992**, *494*, 50.
2. Grodner, J.; Urbański, R.; Bełżecki, C.; Chmielewski, M. *Polish J. Chem.* **1992**, *66*, 813.
3. Chmielewski, M.; Grodner, J.; Wang Fudong; Urbańczyk-Lipkowska, Z. *Tetrahedron* **1992**, *48*, 2935; Chmielewski, M.; Grodner, J. *J. Carbohydr. Chem.* **1992**, *11*, 691.
4. Chmielewski, M.; Kałuża, Z.; Abramski, W.; Bełżecki, C. *Tetrahedron Lett.* **1987**, *28*, 3035.
5. Chmielewski, M.; Kałuza, Z.; Abramski, W.; Grodner, J.; Bełżecki, C.; Sedmera, P. *Tetrahedron* **1989**, *45*, 227.
6. Fürstner, A.; Weidmann, H. *J. Carbohydr. Chem.* **1988**, *7*, 773, and references cited therein.
7. Abramski, W.; Chmielewski, M. *J. Carbohydr. Chm.* To be published.
8. Chmielewski, M.; Kałuża, Z. *Carbohydr. Res.* **1987**, *167*, 143; Chmielewski, M.; Kałuża, Z.; Abramski, W.; Mostowicz, D.; Hintze, B.; Bełżecki, C. *Bull. Poll. Ac. Chem.* **1987**, *35*, 245.
9. Selected analytical and spectral data:

10: mp, 148-150 °C; $[\alpha]_D$ -41.4° (*c* 1, $CHCl_3$); IR ($CHCl_3$): 3215 (NH), 1780 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): 1.38, 1.43 (2s, 6H,isopropylidene), 3.85 (t, 1H, $J_{1,2}$ = 3.0 and $J_{2,NH}$ = 2.2 Hz, H-2), 3.99 (dd, 1H, $J_{5,6}$ = 5.8 and $J_{6,6'}$ = 8.3 Hz, H-6), 4.11 (dd, 1H, $J_{5,6'}$ = 6.3 Hz, H-6'), 4.30 (d, 1H, $J_{3,4}$ = 3.6 Hz, H-3), 4.33 (dd, 1H, $J_{4,5}$ = 6.7 Hz, H-4), 4.46 (q, 1H, H-5), 4.54, 4.60 (2d, 2H, *J* = 11.7 Hz, benzyl), 5.72 (d, 1H, H-1), 6.07 (bs, 1H, NH); MS (m/z): $(M+1)^+$ = 319.

Compound **11** was acetylated to afford **13** which was characterized: mp, 120-121 °C; $[\alpha]_D$ - 32.5° (*c* 1, CH_2Cl_2); IR ($CHCl_3$): 3210 (NH), 1780 (C=O), 1735 cm^{-1} (C=O); ^1H NMR ($CDCl_3$): 2.08, 2.11 (2s, 6H, 2Ac), 3.90 (m, 1H, H-2), 4.23 (dd, 1H, $J_{4,5}$ = 5.0 and $J_{5,5'}$ = 11.8 Hz, H-5), 4.39 (dd, 1H, $J_{4,5'}$ = 6.0 Hz, H-5'), 4.61 (m, 1H, $J_{2,4}$ = $J_{3,4}$ = 1.1 Hz, H-4), 5.36 (s, 1H, H-3), 5.79 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1), 6.23 (bs, 1H, NH); MS (m/z): $(M+1)^+$ = 244.

12: mp, 86-87 °C; $[\alpha]_D$ -140.0° (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$): 3.49 (dd, 1H, $J_{4,5}$ = 7.5, $J_{5,5'}$ = 9.8 Hz, H-5), 3.59 (dd, 1H, $J_{4,5'}$ = 6.0 Hz, H-5'), 3.87 (m, 1H, H-2), 4.26 (bs, 1H, H-3), 4.50 (s, 2H, benzyl), 4.54 (m, 2H, benzyl), 4.70 (m, 1H, $J_{2,4}$ = $J_{3,4}$ = 1.1 Hz, H-4), 5.73 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1), 6.08 (bs, 1H, NH); MS (m/z): $(M+1)^+$ = 340.

10. Urbańczyk-Lipkowska, Z.; Abramski, W.; Chmielewski, M. To be published elsewhere.