Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 2561–2563

TETRAHEDRON LETTERS

Dehydrative glycosylation of tri-*O*-benzylated 1-hydroxyribofuranose catalyzed by a copper(II) complex

Takeyuki Suzuki, Shoko Watanabe, Taichiro Yamada and Kunio Hiroi*

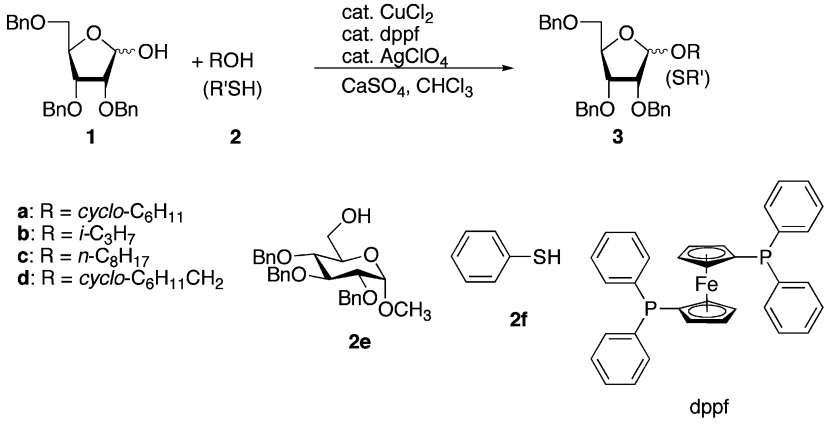
Department of Synthetic Organic Chemistry, Tohoku Pharmaceutical University, 4-4-1 Komatsushima, Aoba-Ku, Sendai 981-8558, Japan

Received 7 January 2003; revised 27 January 2003; accepted 29 January 2003

Abstract—A phosphine/Cu(II) complex catalyzes the dehydrative glycosylation of tri-*O*-benzylated 1-hydroxyribofuranose to give the ribofuranoside with high stereoselectivity.

The development of efficient stereoselective glycosylations is one of the most important subjects in carbohydrate chemistry.[1] Although the direct glycosylation of 1-hydroxy sugars is highly desirable,[2] there are only a few examples of catalytic dehydrative glycosylations. Inanaga reported that methoxyacetic acid/$Yb(OTf)_3$ (10 mol%) promotes the reaction of 1-hydroxy sugars with alcohols to afford the glycosides in 72–99% yield with moderate to excellent selectivities.[3] Mukaiyama developed some elegant methods for the stereoselective synthesis of both 1,2-*cis*- and *trans*-ribofuranosides from 1-hydroxyribofuranoses and alcohols or trimethylsilyl ethers using $Ph_2Sn{=}S$ (20 mol%)/$AgClO_4$,[4] Lawesson's reagent (10 mol%)/$AgClO_4$,[4] M(OTf)n (1 mol%)/hexamethyldisiloxane (M = Sn, La, and Yb),[5] and $TrB(C_6F_5)_4$ (3 mol%).[6] We report a new protocol using a phosphine Cu(II) catalyst that gives the ribofuranosides with reasonable selectivity (Scheme 1).

When a mixture of 2,3,5-tri-*O*-benzyl-D-ribofuranose (**1**)[7] and cyclohexanol (**2a**) and a catalyst system prepared from $CuCl_2$, bis(diphenylphosphino)ferrocene (dppf), and $AgClO_4$ (1:1:2 mol ratio) in $CHCl_3$ in the presence of $CaSO_4$ as a dehydrating agent (**1**:**2a**:Cu:Ca = 100:120:5:1000 mol ratio) was allowed to stand at room temperature for 21 h, cyclohexyl 2,3,5-tri-*O*-benzyl-D-ribofuranoside (**3a**)[2c] was obtained in 95% yield (α:β = 5:95). No reaction occurred without $CuCl_2$ or $AgClO_4$ under otherwise identical conditions. The use of CuCl instead of $CuCl_2$ also afforded no reaction. Changing the Cu/$AgClO_4$ ratio affected the reactivity. The catalyst prepared with a Cu/dppf/



Scheme 1. Dehydrative glycosylation of 2,3,5-tri-*O*-benzyl-D-ribofuranose **1**.

* Corresponding author. Tel.: +81 22 234 4181 (ext. 2531); fax: +81 22 275 2013; e-mail: khiroi@tohoku-pharm.ac.jp

0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00270-3

Table 1. Dehydrative glycosylation of **1** catalyzed by a Cu(II) complex[a]

Entry	Acceptor	Additive	Time (h)	Ribofuranoside		
				No.	Yield[b] (%)	α/β[c]
1	**2a**	None	21	**3a**	95	5:95
2	**2a**	$LiClO_4$	7	**3a**	90	96:4
3	**2b**	None	22	**3b**	85	10:90
4	**2b**	$LiClO_4$	3	**3b**	87	88:12
5	**2c**	None	22	**3c**	80	15:85
6	**2c**	$LiClO_4$	6	**3c**	97	93:7
7	**2d**	None	16	**3d**	77	19:81
8	**2d**	$LiClO_4$	5	**3d**	92	92:8
9	**2e**	None	19	**3e**	77	25:75
10	**2e**	$LiClO_4$	7	**3e**	82	98:2
11	**2f**	None	19	**3f**	68	93:7[d]
12	**2f**	$LiClO_4$	19	**3f**	89	71:29[d]

[a] The reaction was conducted at room temperature using 0.100 mmol of **1**, 0.120 mmol of **2**, 1.00 mmol of $CaSO_4$, and 0.150 mmol of additive in $CHCl_3$ (0.02 M) containing 5 mol% of the catalyst.
[b] Isolated yield.
[c] HPLC analysis using a Tosoh TSKgel Silica-60 column unless otherwise specified.
[d] Determined by ^1H NMR analysis.

$AgClO_4$ (1:1:1 mol ratio) gave a lower yield of 39%. These results suggest that $Cu(ClO_4)_2$ is an active catalyst. In fact, $Cu(ClO_4)_2{\cdot}6H_2O$ could be used in place of $CuCl_2$–$AgClO_4$. Other silver salts such as AgOTf, $AgBF_4$, $AgPF_6$, and $AgSbF_6$ gave less satisfactory results. The activity of $CuCl_2$–$AgClO_4$ was enhanced by the addition of 1 equiv. of dppf at the early stage of the reaction. The yield after 1 h was increased from 13 to 87%.[8] Although other phosphine ligands such as dppp and dppb showed similar reactivities and selectivities, the addition of bipyridine completely retarded the reaction. It is noteworthy that reversed stereoselectivity was obtained by the addition of 1.5 equiv. of $LiClO_4$ to the catalyst system.[9] Thus, the addition of $LiClO_4$ to the reaction mixture of **1** and **2a** afforded **3a** in 90% yield (α:β = 96:4).

Table 1 shows some examples of the dehydrative glycosylation of **1** with various glycosyl acceptors using the phosphine/Cu catalyst.[10] The reaction of *i*-C_3H_7OH **2b** gave the ribofuranoside **3b** in 85% yield (α:β = 10:90, entry 3). Primary alcohols **2c**, **2d** and **2e** can be used as glycosyl acceptors to give **3c**, **3d**[2c] and **3e**,[11] although the extent of β-selectivity is less satisfactory (entries 5, 7 and 9). However, The reaction of **2e** in the presence of $LiClO_4$ gave **3e** with the highest α-selectivity (entry 10). Interestingly, the reaction of thiophenol afforded the corresponding α-ribofuranoside **3f**[12] preferentially with or without $LiClO_4$ (entries 11 and 12).

In summary, a Cu(II)-catalyzed dehydrative glycosylation of tri-*O*-benzylated 1-hydroxyribofuranose was developed for the first time. The properties of the Cu(II) catalysts should be readily modifiable to afford more efficient catalysts, because various phosphine ligands are available. Our results should provide a basis for designing more efficient catalyst systems.

References

1. For reviews, see: (a) Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503–1531; (b) Davis, B. G. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3215–3237; (c) Davis, B. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2137–2160.
2. For recent examples of dehydrative glycosylations, see: (a) Nguyen, H. M.; Chen, Y.; Duron, S. G.; Gin, D. Y. *J. Am. Chem. Soc.* **2001**, *123*, 8766–8772; (b) Nguyen, H. M.; Poole, J. L.; Gin, D. Y. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 414–417; (c) Hirooka, M.; Mori, Y.; Sasaki, A.; Koto, S.; Shinoda, Y.; Morinaga, A. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1679–1694 and references cited therein; (d) Hirooka, M.; Terayama, M.; Mitani, E.; Koto, S.; Miura, A.; Chiba, K.; Takabatake, A.; Tashiro, T. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1301–1309.
3. Inanaga, J.; Yokoyama, Y.; Hanamoto, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1090–1091.
4. Shimomura, N.; Mukaiyama, T. *Chem. Lett.* **1993**, 1941–1944.
5. Mukaiyama, T.; Matsubara, K.; Hora, M. *Synthesis* **1994**, 1368–1373.
6. (a) Uchiro, H.; Mukaiyama, T. *Chem. Lett.* **1996**, 79–80; (b) Uchiro, H.; Mukaiyama, T. *Chem. Lett.* **1996**, 271–272.
7. Barker, R.; Fletcher, H. G. *J. Org. Chem.* **1961**, *26*, 4605–4609.
8. Time-course experiment showed that selectivity was increased gradually (α:β = 28:72, after 10 min (11% yield), then 10:90, after 30 min (69% yield), and α:β = 8:92, after 1 h (87% yield)). These results indicate that the prolonged exposure of the product to the reaction conditions afforded the partial anomerization of α-anomer to thermodynamically more stable β-anomer.
9. For the effects of $LiClO_4$ on stereoselective glycosylation, see: Mukaiyama, T.; Kobayashi, S.; Shoda, S. *Chem. Lett.* **1984**, 907–910.

10. General procedure for glycosylation of **1** using Cu(II) catalyst: To a stirred suspension of $CuCl_2$ (0.7 mg, 0.005 mmol), dppf (2.8 mg, 0.005 mmol), $AgClO_4$ (2.1 mg, 0.010 mmol) and $CaSO_4$ (136 mg, 1.0 mmol) in $CHCl_3$ (2 mL) was added a solution of **1** (42.1 mg, 0.1 mmol) and **2** (0.12 mmol) in $CHCl_3$ (3 mL) at room temperature. After the time shown in Table 1, the mixture was diluted with ether and the solution was passed through a Celite pad, and concentrated under reduced pressure. The resulting crude product was purified by flash chromatography on silica gel. Spectral data for **3b**. α-Anomer: $[\alpha]_D^{26}$ +57.1 (*c* 1.19 $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.22 (d, $J=6.1$ Hz, 3H), 1.29 (d, $J=6.1$ Hz, 3H), 3.36 (dd, $J=10.5$, 4.1 Hz, 1H), 3.45 (dd, $J=10.6$, 3.6 Hz, 1H), 3.75 (dd, $J=6.6$, 4.1 Hz, 1H), 3.82 (dd, $J=6.8$, 4.0 Hz, 1H), 3.96 (sep., $J=6.1$ Hz, 1H), 4.23 (q, $J=3.8$ Hz, 1H), 4.4–4.8 (m, 6H), 5.11 (d, $J=4.0$ Hz, 1H), 7.2–7.4 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.76, 23.65, 69.97, 70.00, 72.17, 72.35, 73.39, 75.41, 77.41, 81.02, 99.68, 127.48, 127.58, 127.62, 127.68, 127.98, 128.05, 128.19, 128.30, 128.32, 138.05, 138.13, 138.55; IR (neat) 3088, 3063, 3030, 2971, 2922, 2866, 1605, 1497, 1454, 1366, 1331, 1258, 1208, 1113, 1028, 737, 698; MS (EI) *m*/*z* 91 (Bn, base peak), 462 (M^+); HRMS (EI); calcd for $C_{29}H_{34}O_5$ 462.2406 found 462.2413. β-Anomer: $[\alpha]_D^{26}$ +2.8 (*c* 1.06 $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.09 (d, $J=6.1$ Hz, 3H), 1.10 (d, $J=6.1$ Hz, 3H), 3.52 (dd, $J=10.5$, 6.0 Hz, 1H), 3.60 (dd, $J=10.5$, 4.1 Hz, 1H), 3.82 (bd, $J=4.8$ Hz, 1H), 3.88 (sep., $J=6.1$ Hz, 1H), 3.99–4.03 (m, 1H), 4.3–4.4 (m, 1H), 4.4–4.7 (m, 6H), 5.11 (s, 1H), 7.2–7.4 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.33, 23.42, 69.26, 71.74, 72.39(2C), 73.16, 78.81, 80.23, 80.31, 103.33, 127.50, 127.67, 127.70, 127.76, 127.81, 127.96, 128.29, 128.34, 128.39, 137.99, 138.02, 138.35; IR (neat) 3088, 3063, 3030, 2971, 2926, 2863, 1605, 1497, 1454, 1368, 1308, 1262, 1208, 1124, 1096, 1028, 737, 698; MS (EI) *m*/*z* 91 (Bn, base peak), 462 (M^+); HRMS (EI); calcd for $C_{29}H_{34}O_5$ 462.2406, found 462.2419. **3c**. α-Anomer: $[\alpha]_D^{22}$ +81.4 (*c* 1.57, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, $J=$ 6.9 Hz, 3H), 1.26 (s, 12H), 3.37 (dd, $J=10.4$, 4.1 Hz, 1H), 3.45 (dd, $J=10.5$, 3.6 Hz, 1H), 3.52 (dt, $J=9.9$, 6.8 Hz, 1H), 3.7–3.85 (m, 3H), 4.23 (q, $J=4.0$ Hz, 1H), 4.2–4.75 (m, 6H), 5.00 (d, $J=4.1$ Hz, 1H), 7.1–7.4 (m, 15H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.21, 22.76, 26.23, 29.39, 29.50, 29.72, 31.92, 68.48, 70.02, 72.21, 72.45, 73.40, 75.36, 81.34, 101.30, 127.43, 127.53, 127.60, 127.87, 127.99, 128.11, 128.19, 128.23, 137.89, 137.93, 138.31; IR (neat) 3088, 3063, 3030, 2926, 2857, 1607, 1497, 1454, 1360, 1331, 1258, 1208, 1115, 1080, 1044, 1028, 737, 698; MS (EI) *m*/*z* 91 (Bn, base peak), 532 (M^+); HRMS (EI); calcd for $C_{34}H_{44}O_5$ 532.3189, found 532.3197. β-Anomer: $[\alpha]_D^{24}$ −21.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, $J=6.4$ Hz, 3H), 1.25 (s, 12H), 3.32 (dt, $J=9.6$, 6.8 Hz, 1H), 3.51 (dd, $J=10.6$, 5.9 Hz, 1H), 3.61 (dd, $J=10.6$, 4.0 Hz, 1H), 3.66 (dt, $J=9.6$, 6.8 Hz, 1H), 3.86 (dd, $J=4.8$, 1.2 Hz, 1H), 4.01 (dd, $J=6.9$, 4.6 Hz, 1H), 4.33 (m, 1H), 4.4–4.9 (m, 6H), 5.00 (d, $J=1.2$ Hz, 1H), 7.2–7.4 (m, 15H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.20, 22.74, 26.17, 29.32, 29.45, 29.57, 31.90, 68.00, 71.57, 72.27, 72.38, 73.14, 78.69, 79.86, 80.32, 105.25, 127.37, 127.49, 127.60, 127.65, 127.71, 127.82, 128.17, 128.21, 128.26, 137.79, 137.82, 138.22; IR (neat) 3063, 3030, 2926, 2857, 1607, 1497, 1454, 1360, 1308, 1260, 1208, 1105, 735, 698; MS (EI) *m*/*z* 91 (Bn, base peak), 532 (M^+); HRMS (EI); calcd for $C_{34}H_{44}O_5$ 532.3189 found 532.3188.
11. Shimomura, N.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2532–2541.
12. Kametani, T.; Kawamura, K.; Honda, T. *J. Am. Chem. Soc.* **1987**, *109*, 3010–3017.