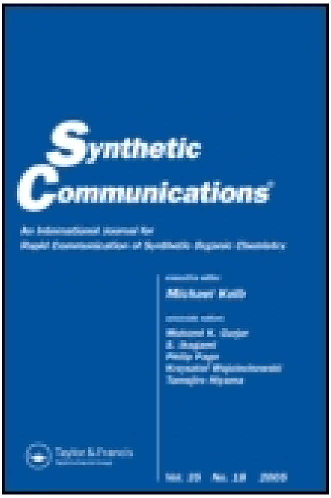


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Monobenzylation Of 1,n-Diols via Dibutylstannylene Intermediates

Eugene A. Mash [a] , Liza T. A. Kantor [a] & Stephen C. Waller [a]

[a] Department of Chemistry , The University of Arizona , Tucson, Arizona, 85721, USA

To cite this article: Eugene A. Mash , Liza T. A. Kantor & Stephen C. Waller (1997) Monobenzylation Of 1,n-Diols via Dibutylstannylene Intermediates, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 27:3, 507-514, DOI: 10.1080/00397919708006052

To link to this article: http://dx.doi.org/10.1080/00397919708006052

SYNTHETIC COMMUNICATIONS, 27(3), 507-514 (1997)

MONOBENZYLATION OF 1,*n*-DIOLS VIA DIBUTYLSTANNYLENE INTERMEDIATES

Eugene A. Mash*, Liza T. A. Kantor, and Stephen C. Waller

Department of Chemistry, The University of Arizona, Tucson, Arizona 85721
USA

Abstract: Symmetrical primary 1,*n*-diols, $HO(CH_2)_nOH$, of any chain length from n = 2-10, can be selectively monobenzylated via sequential treatment with dibutyltin oxide and benzyl bromide.

In the context of another problem, we required quantities of monobenzyl ethers **2** derived from symmetric 1,*n*-diols **1**. Previous strategies for the selective monoprotection of symmetric diols have included the use of excess diol,[1] the use of polymer-bound intermediates,[2] the use of thallium salts,[3] and the use of monosodium salts.[4] For expensive compounds, the use of excess diol is impractical and could make purification of **2** more difficult. The use of polymer-bound intermediates would necessarily involve multiple synthetic steps, and could

$$\underset{\mathbf{1}}{HO(CH_2)_nOH} \xrightarrow[\text{base}]{C_6H_5CH_2X} \underset{\mathbf{2}}{HO(CH_2)_nOCH_2C_6H_5}$$

---

*Author to whom correspondence should be addressed limit the throughput of material. The use of large quantities of thallous ethoxide, which is both toxic and expensive, was unappealing. The benzylation of the monosodium salt, while conceptually simple, has in practice produced variable results.[5] These considerations prompted a search for an alternative synthesis.

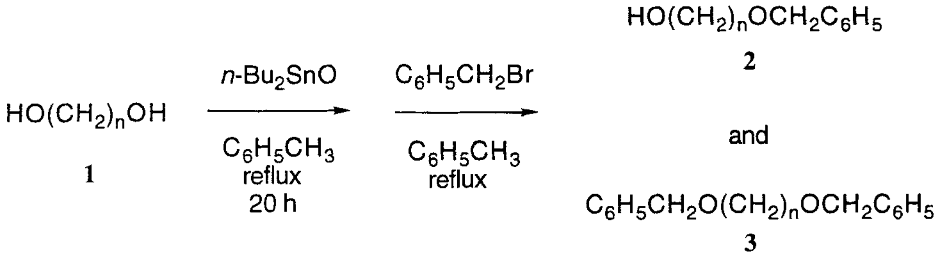
Preparations and monoalkylations of *O*-stannylene acetals have been widely employed for selective protection of carbohydrate 1,2-diols.[6] While *O*-stannylene acetals of several simple 1,*n*-diols have been reported,[7] alkylations of these compounds have not been systematically examined.

Reactions of 1,*n*-alkanediols **1a-i** (see Table) with 1 equivalent of dibutyltin oxide in toluene at reflux with azeotropic removal of water gave clear solutions after 20 hours. One or two equivalents of benzyl bromide and 40 mole % of tetra-*N*-butylammonium bromide were then added, and reflux was continued for a time prior to workup and isolation of products.

Benzylations of the stannylene intermediates derived from shorter diols were more rapid, but remarkably, monobenzylation was achieved in greater than statistical yields for nearly every diol examined. The use of excess benzyl bromide was unnecessary (compare entries 3 and 4), and simply complicated the purification of the monobenzylated products **2**. For only two diols (**1g** and **1i**, entries 9 and 12) were the isolated yields of monobenzylated product $\leq 50\%$. In these cases, benzylation was slow, and considerable diol remained in evidence by thin layer chromatography at the time of quench. Smaller amounts of dibenzyl ethers **3** were also observed as byproducts by thin layer chromatography. In one case (entry 7) the dibenzyl ether **3e** was isolated and characterized.[8] In no case has this benzylation procedure been fully optimized. The use of other electrophiles has not been explored.

In summary, the benzylation of symmetric 1,*n*-diols via *O*-stannylene intermediates appears general, although the nature(s) of the reactive stannylene

Table. Monobenzylations of Symmetrical Primary 1,*n*-Diols.



Entry	Diol	n	Time of Reaction, hours	Products	Yields, %
1[a]	**1a**	2	1	**2a**	65
2[a]	**1b**	3	1	**2b**	69
3[a]	**1c**	4	1	**2c**	30
4	**1c**	4	47	**2c**	58
5	**1d**	5	1	**2d**	16
6	**1d**	5	20	**2d**	56
7	**1e**	6	142	**2e**	64
				3e	22
8	**1f**	7	142	**2f**	71
9	**1g**	8	143	**2g**	46
10	**1h**	9	16	**2h**	38
11	**1h**	9	118	**2h**	57
12	**1i**	10	143	**2i**	50

[a] Two equivalents of $C_6H_5CH_2Br$ were employed.

intermediates derived from the longer diols remain unclear. Studies to explore further the reactivities of these intermediates may lead to other useful desymmetrized reagents.

General Procedures. All reactions were run under an argon atmosphere. Reagents, including the precursor diols **1a-i**, were purchased from Aldrich Chemical Company and were used without further purification, with the exception of benzyl bromide, which was distilled from calcium hydride. Analytical thin-layer chromatography (tlc) employed Merck glass-backed pre-coated plates (0.25 mm, silica gel 60, F-254). Column chromatography was carried out on silica gel 60 (Merck, 70-200 mesh). ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ with Me_4Si as an internal standard. Spectra of known compounds matched the previously reported data.[9-16] High resolution mass spectra were recorded at the Nebraska Center for Mass Spectrometry, Lincoln, Nebraska. Elemental analyses were performed by Desert Analytics, Tucson, Arizona.

General Procedure for the Preparation of Monobenzylated Diols. To a solution of the diol (4.02 mmol) in toluene (60 mL) was added dibutyltin oxide (1.00 g, 4.02 mmol). The mixture was heated at reflux under a Dean Stark apparatus for 20 h. The Dean Stark trap was emptied, and benzyl bromide (480 µL, 4.02 mmol) and tetrabutylammonium bromide (520 mg, 1.61 mmol) were added to the reaction mixture. Reflux was resumed until the Dean Stark trap filled, at which time it was emptied and removed from the system. The reaction mixture was heated at reflux for a time, then cooled and concentrated *in vacuo*. The residue was chromatographed on silica gel 60 (approximately 130 g) using a mixture of ethyl acetate and hexanes (generally 40%) as eluent. Product yields are given in the Table and spectroscopic data are listed below.

2-(Phenylmethoxy)ethanol (2a).[9] ^{1}H NMR δ 2.83 (1, s), 3.55 (2, t, J = 4 Hz), 3.72 (2, t, J = 4 Hz), 4.52 (2, s), 7.20-7.40 (5, m); ^{13}C NMR δ 61.6

(CH_2), 71.4 (CH_2), 73.1 (CH_2), 127.7 (CH), 127.8 (CH), 128.3 (CH), 137.9 (C).

3-(Phenylmethoxy)propan-1-ol (2b).[9,10] ^{1}H NMR δ 1.75-1.90 (2, m), 2.62 (1, s), 3.64 (2, t, J = 6 Hz), 3.75 (2, t, J = 6 Hz), 4.50 (2, s), 7.20-7.40 (5, m); ^{13}C NMR δ 32.1 (CH_2), 61.6 (CH_2), 69.2 (CH_2), 73.2 (CH_2), 127.7 (CH), 128.4 (CH), 128.5 (CH), 138.8 (C).

4-(Phenylmethoxy)butan-1-ol (2c).[11] ^{1}H NMR δ 1.55-1.75 (4, m), 2.54 (1, s), 3.50 (2, t, J = 6 Hz), 3.61 (2, t, J = 6 Hz), 4.51 (2, s), 7.20-7.40 (5, m); ^{13}C NMR δ 26.6 (CH_2), 30.0 (CH_2), 62.5 (CH_2), 70.3 (CH_2), 73.0 (CH_2), 127.7 (CH), 127.8 (CH), 128.4 (CH), 139.0 (C).

5-(Phenylmethoxy)pentan-1-ol (2d).[12] ^{1}H NMR δ 1.35-1.75 (6, m), 2.23 (1, s), 3.45 (2, t, J = 6.6 Hz), 3.57 (2, t, J = 6.7 Hz), 4.49 (2, s), 7.22-7.42 (5, m); ^{13}C NMR δ 22.4 (CH_2), 29.4 (CH_2), 32.4 (CH_2), 62.7 (CH_2), 70.3 (CH_2), 72.9 (CH_2), 127.5 (CH), 127.6 (CH), 128.3 (CH), 138.5 (C).

6-(Phenylmethoxy)hexan-1-ol (2e).[13] ^{1}H NMR δ 1.30-1.70 (8, m), 3.30 (1, br s), 3.47 (2, t, J = 6.4 Hz), 3.60 (2, t, J = 6.4 Hz), 4.50 (2, s), 7.20-7.40 (5, m); ^{13}C NMR δ 25.5 (CH_2), 25.9 (CH_2), 29.6 (CH_2), 32.5 (CH_2), 62.8 (CH_2), 70.3 (CH_2), 72.8 (CH_2), 127.5 (CH), 127.6 (CH), 128.3 (CH), 138.5 (C).

1,6-Hexanediol Dibenzyl Ether (3e).[14] IR (neat) 3066 (w), 3027 (w), 2931, 2854, 1451, 1361, 1100; ^{1}H NMR δ 1.39-1.45 (4, m), 1.61-1.68 (4, m), 3.49 (4, t, J = 6.5 Hz), 4.52 (4, s), 7.26-7.37 (10, m); ^{13}C NMR δ 26.0 (CH_2), 29.7 (CH_2), 70.3 (CH_2), 72.8 (CH_2), 127.4 (CH), 127.6 (CH), 128.3 (CH), 138.6 (C); mass spectrum (70 eV) m/z (rel. int.) 207 (2), 123 (2), 107 (16), 91 (100).

Anal. Calcd for $C_{20}H_{26}O_2$: C 80.50, H 8.78; found: C 80.51, H 8.72.

7-(Phenylmethoxy)heptan-1-ol (2f). IR (neat) 3384 (br), 3060 (w), 2930, 2854, 1494, 1451, 1098; ^{1}H NMR δ 1.25-1.50 (6, m), 1.45-1.70 (4, m), 2.45 (1, br s), 3.46 (2, t, J = 6.5 Hz), 3.61 (2, t, J = 6.5 Hz), 4.50 (2, s), 7.20-7.40 (5, m); ^{13}C NMR δ 25.6 (CH_2), 26.1 (CH_2), 29.2 (CH_2), 29.6 (CH_2), 32.6 (CH_2), 62.9 (CH_2), 70.4 (CH_2), 72.9 (CH_2), 127.5 (CH), 127.6 (CH), 128.3 (CH), 138.5 (C); mass spectrum (70 eV) m/z (rel. int.) 222 (1), 123 (3), 107 (41), 91 (100); HRMS calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1615.

Anal. Calcd for $C_{14}H_{22}O_2$: C 75.63, H 9.97; found: C 74.73, H 9.88.

8-(Phenylmethoxy)octan-1-ol (2g).[15] ^{1}H NMR δ 1.25-1.45 (8, m), 1.45-1.70 (4, m), 2.15 (1, br s), 3.47 (2, t, J = 6.9 Hz), 3.59 (2, t, J = 6.4 Hz), 4.50 (2, s), 7.22-7.42 (5, m); ^{13}C NMR (resolved lines) δ 25.7 (CH_2), 26.1 (CH_2), 29.4 (CH_2), 29.7 (CH_2), 32.7 (CH_2), 62.8 (CH_2), 70.5 (CH_2), 72.8 (CH_2), 127.5 (CH), 127.6 (CH), 128.3 (CH), 138.6 (C).

9-(Phenylmethoxy)nonan-1-ol (2h). IR (neat) 3385 (br), 3029 (w), 2927, 2852, 1494, 1452, 1362, 1100; ^{1}H NMR δ 1.15-1.45 (10, m), 1.45-1.70 (5, m), 3.46 (2, t, J = 6.6 Hz), 3.61 (2, t, J = 6.4 Hz), 4.51 (2, s), 7.20-7.40 (5, m); ^{13}C NMR (resolved lines) δ 25.7 (CH_2), 26.1 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.7 (CH_2), 32.7 (CH_2), 62.9 (CH_2), 70.5 (CH_2), 72.8 (CH_2), 127.5 (CH), 127.6 (CH), 128.3 (CH), 138.6 (C); mass spectrum (70 eV) m/z (rel. int.) 250 (1), 123 (1), 107 (45), 91 (100).

Anal. Calcd for $C_{16}H_{26}O_2$: C 76.75, H 10.47; found: C 76.74, H 10.17.

10-(Phenylmethoxy)decan-1-ol (2i).[16] ^{1}H NMR δ 1.20-1.50 (12, m), 1.50-1.70 (5, m), 3.47 (2, t, J = 6.4 Hz), 3.62 (2, t, J = 6.4 Hz), 4.51 (2, s), 7.22-7.42 (5, m); ^{13}C NMR (resolved lines) δ 25.7 (CH_2), 26.2 (CH_2), 29.5 (CH_2), 29.7 (CH_2), 32.8 (CH_2), 63.0 (CH_2), 70.5 (CH_2), 72.9 (CH_2), 127.5 (CH), 127.6 (CH), 128.3 (CH), 138.7 (C).

Acknowledgment. Partial support of this research by Research Corporation and by the University of Arizona through the Materials Characterization Program, the Office of the Vice President for Research, and the Department of Chemistry is gratefully acknowledged.

References

1. (a) Sheehan, M., Spangler, R. J., and Djerassi, C. *J. Org. Chem.* **1971**, *36*, 3526. (b) Trost, B. M., and Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4743. (c) Ikeda, J., Ikeda, N., and Yamamoto, H. *Tetrahedron Lett.* **1984**, *25*, 5177.
2. Leznoff, C. C. *Acc. Chem. Res.* **1978**, *11*, 327 and references cited therein.
3. Kalinowski, H.-O., Crass, G., and Seebach, D. *Chem. Ber.* **1981**, *114*, 477.
4. McDougal, P. G., Rico, J. G., Oh, Y.-I., and Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388.
5. For examples, see: (a) Collins, P. M. , and Eder, H. *J. Chem. Soc., Perkin Trans. I* **1984**, 1525. (b) Baxter, A. D., Binns, F., Javed, T., Roberts, S. M., Sadler, P., Scheinmann, F., Wakefield, B. J., Lynch, M., and Newton, R. F. *J. Chem. Soc., Perkin Trans. I* **1986**, 889. (c) Fredriksen, S. B., and Dale, J. *Acta. Chem. Scand.* **1992**, *46*, 574. (d) Lehmann, J., and Petry, S. *Liebigs Ann. Chem.* **1993**, 1111.
6. David, S., and Hanessian, S. *Tetrahedron* **1985**, *41*, 643 and references cited therein.
7. The structures of the *O*-stannylene intermediates are diol-dependent and are commonly aggregated; see Reference 6 and (a) Considine, J. *J. Organometal. Chem.* **1966**, *5*, 263. (b) Pommier, J.-C., and Valade, J.

J. Organometal. Chem. **1968**, *12*, 433. (c) Smith, P. J., White, R. F. M., and Smith, L. *J. Organometal. Chem.* **1972**, *40*, 341.

8. Dibenzyl ethers **3** were normally obtained contaminated with benzyl bromide during the chromatographic purification of monobenzyl ethers **1** and were not normally further purified or characterized.
9. Kotsuki, H., Ushio, Y., Yoshimura, N., and Ochi, M. *J. Org. Chem.* **1987**, *52*, 2594.
10. Gennari, C., and Cozzi, P. G. *J. Org. Chem.* **1988**, *53*, 4015.
11. Thies, H., Wolfschutz, R., Frenking, G., Schmidt, J., and Schwarz, H. *Tetrahedron* **1982**, *38*, 1647.
12. Börjesson, L., Csöregh, I., and Welch, C. J. *J. Org. Chem.* **1995**, *60*, 2989.
13. Halcomb, R. L., Huang, H., and Wong, C.-W. *J. Am. Chem. Soc.* **1994**, *116*, 11315.
14. (a) De la Zerda, J., Barak, G., and Sasson, Y. *Tetrahedron* **1989**, *45*, 1533. (b) Vinczer, P., Aesa, M., Sztruhar, S., Barbier, V., and Novak, L. *Magy. Kem. Foly.* **1993**, *99*, 443; *Chem. Abstr.* **1994**, *120*, 269737w.
15. Czech, B. P., and Bartsch, R. A. *J. Org. Chem.* **1984**, *49*, 4076.
16. Matsuura, H., Yoshihara, T., and Ichihara, A. *Biosci. Biotech. Biochem.* **1993**, *57*, 1492.

(Received in the USA 16 August 1996)