Deiodination Reactions using Tributyltin Hydride for Potential Labelling Experiments

Elizabeth M. Zippi,*† Gary W. Plourde, II† and N. Satyamurthy§

†Department of Physical Sciences, Kutztown University, Kutztown, PA 19530, U.S.A.

§UCLA Biomedical Cyclotron, Los Angeles, CA 90024, U.S.A.

Summary

2,6-Dinitro-1-iodobenzene and 2,4-dinitro-1-iodobenzene were deiodinated with tributyltin hydride at different temperatures using various addition modes. The product ratios of 1,3-dinitrobenzene and the corresponding tributylstannyldinitrobenzene compounds were determined by NMR in order to evaluate the optimum conditions for impending tritiation experiments.

Key Words: Deiodination, Tributyltin hydride, Tritiation, Aryltributyltin

Introduction

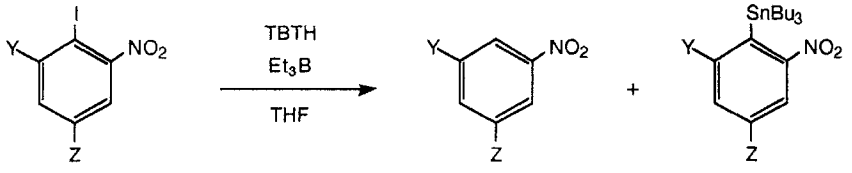
Tributyltin tritide, prepared in high yield at high specific activity by the treatment of Li^3H (synthesized from carrier-free tritium gas) with tributyltin chloride (1) shows promise as a useful tritiation reagent (2). Little has been accomplished using tributyltin tritide prepared via the earlier, well-established methods (3) due to the lower specific activity of the reagent. Tributyltin hydride is an easily prepared, (4, 5) relatively stable, versatile reagent with a toxicity level within the required limits (5). Among the many uses of tributyltin hydride is the hydrogenolysis of aromatic halides via dehalogenation (6, 7). Requirements for a dehalogenation reaction are that the substrate contains a good leaving group (I>Br>Cl) (8, 9) and strong electron withdrawing groups located *ortho-* or *para-* to the halogen (9) for activation of the leaving group.

*Author for correspondence. Present address: Department of Chemistry and Physics, Louisiana State University, Shreveport, LA 71115, U.S.A.

CCC 0362–4803/95/040361–04

Received 30 August, 1994
Revised 1 November, 1994

In order to determine ideal tritiation conditions when using tributyltin tritide, a number of experiments were carried out using tributyltin hydride (TBTH) with triethylborane (Et_3B) as a catalyst. Deiodinations of 2,6-dinitro-1-iodobenzene were accomplished at room temperature and at -78 °C, varying the mode of addition of reagents (Scheme 1a, Table 1). Similar deiodinations of 2,4-dinitro-1-iodobenzene were achieved at room temperature and at -10 °C, varying the manner in which the reagents were added (Scheme 1b, Table 2).



I-DNB DNB Bu_3Sn-DNB

Scheme 1a: Y = NO_2 , Z = H

Scheme 1b: Y = H , Z = NO_2

Table 1: Deiodination of 2,6-Dinitro-1-iodobenzene using Tributyltin Hydride.

Addition Mode[a]	Temperature (°C)	% DNB	% Bu_3Sn-DNB	Ratio DNB/ Bu_3Sn-DNB	% Conversion
1	25	46	29	1.6	75
2	25	56	42	1.3	98
3	25	46	35	1.3	81
1	-78	40	38	1.1	78
2	-78	43	43	1.0	86

Table 2: Deiodination of 2,4-Dinitro-1-iodobenzene using Tributyltin Hydride.

Addition Mode[a]	Temperature (°C)	% DNB	% Bu_3Sn-DNB	Ratio DNB/ Bu_3Sn-DNB	% Conversion
1	25	33	13	2.5	46
2	25	58	21	2.8	79
3	25	54	15	3.5	69
1	-10	48	18	2.7	66
2	-10	64	23	2.8	87
3	-10	42	17	2.5	59

[a]Mode 1: TBTH was added to I-DNB followed by addition of Et_3B; Mode 2: I-DNB was added to TBTH and Et_3B; Mode 3: A pre-formed solution of TBTH and Et_3B was added to I-DNB. The entries in Tables 1 and 2 are from single studies.

The data in Table 1 suggest that the preferred addition method for deiodination of 2,6-dinitro-1-iodobenzene with tributyltin hydride is Mode 2 at room temperature and, in general, room temperature reactions were found to be superior to reactions conducted at -78 °C. In addition,

when comparing the additions of the reducing agent and catalyst to 2,6-dinitro-1-iodobenzene, Mode 1 surpassed Mode 3, indicating that premixing is ineffective.

For the deiodinations of 2,4-dinitro-1-iodobenzene with tributyltin hydride, the favored approach for reagent addition is Mode 2 at -10 °C, followed closely by Mode 2 at room temperature as shown by the information in Table 1. No significant differences were noted when the temperature was varied; however, reactions at -10 °C are slightly favored over reactions at room temperature. For the reactions at -10 °C, Mode 1 is preferred to Mode 3.

Mode 2, at or slightly below room temperature, appears to be the desired method of reagent addition for deiodination of iododinitrobenzenes using tributyltin hydride. Tritiation of aromatic compounds with the analogous tributyltin tritide might be accomplished by this approach. Furthermore, aryltributyltin compounds prepared in this manner may have application as synthons in the preparation of radiolabelled imaging agents (10, 11).

Experimental

General.

All glassware, syringes and needles were oven-dried prior to use. The NMR spectra were recorded on either a Bruker 300 MHz or 360 MHz NMR spectrometer using $CDCl_3$ as the solvent and TMS as the internal standard. Thin layer chromatographic analyses were performed using Analtech Silica Gel GHLF 250 mm TLC plates using uv detection. The general procedure is reported below.

Deiodination of 2,6-dinitro-1-iodobenzene.

2,6-Dinitro-1-iodobenzene (29.4 mg, 0.10 mmol) was dissolved in THF (100 µL). To this solution was added tributyltin hydride (30 µL, 0.11 mmol) followed by triethylborane (10 µL, 1.0 M in THF) and the reaction mixture was allowed to stir at room temperature. After 30 min., solid potassium fluoride dihydrate (60 mg) was added and the mixture was allowed to stir for an additional 30 min. Ethyl acetate was added for dilution and the organic phase was removed via pipette, filtered through glass wool and dried with a stream of nitrogen to afford 1,3-dinitrobenzene (56%); ^{1}H NMR: δ 9.08 (s, 1H, ortho to both nitro groups), 8.59 (dd, 2H, ortho to each nitro group), 7.82 (t, 1H, meta to both nitro groups), and 1-tributylstannyl-2,6-dinitrobenzene (42%); ^{1}H NMR: δ 8.24 (d, 2H, meta to tributyltin group), 7.61 (t, 1H, para to

tributyltin group), 1.43 (m, 6H, -$CH_2CH_2C\underline{H}_2CH_3$), 1.31 (m, 6H, -$CH_2C\underline{H}_2CH_2CH_3$), 1.11 (t, 6H, -$C\underline{H}_2CH_2CH_2CH_3$), 0.87 (t, 9H, -$CH_2CH_2CH_2C\underline{H}_3$).

Acknowledgments

This research was funded by the National Tritium Labeling Facility at Lawrence Berkeley Laboratory, Berkeley, CA, supported by the Biomedical Research Technology Program, National Center for Research Resources, National Institutes of Health, under Grant P41 RR01237, through the Department of Energy contract DE-AC03-76SF00098 and by the Department of Physical Sciences, Kutztown University, Kutztown, PA. The authors wish to thank Dr. Philip G. Williams and Dr. Hendrik Andres for their valuable discussions and advice and Dr. Edward Simpson for his efforts in the funding of this work.

References

1. Jaiswal D.K., Andres H., Morimoto H. and Williams P.G. - J. Chem. Soc. Chem. Commun. 907 (1993)
2. Jaiswal D.K., Zippi E.M., Morimoto H., Williams P.G. and Andres H. - International Symposium on Tritium Synthesis, NMR and Applications: International Isotope Society and the Kent and Surrey Collaborative Project in Magnetic Resonance, University of Surrey, Guildford, U.K. (1992)
3. Parnes H. and Pease J. - J. Org. Chem. 44: 151 (1979)
4. Four P. and Guibe F. - J. Org. Chem. 46: 4439 (1981)
5. Neumann W.P. - Synthesis 665 (1987)
6. Kuivila H.G. - Synthesis 499 (1970)
7. Neumann W.P. and Hillgartner H. - Synthesis 537 (1971)
8. Miura K., Ichinose Y., Nozaki K., Fugami K., Oshima K. and Utimoto K. - Bull. Chem. Soc. Jpn. 62: 143 (1989)
9. Lorenz D.H., Shapiro P., Stern A. and Becker E.I. - J. Org. Chem. 28: 2332 (1963)
10. Chumpradit S., Kung M-P., Billings J.J. and Kung H.F. - J. Med. Chem. 34: 877 (1991)
11. McBride B.J., Baldwin R.M., Kerr J.M. and Wu J-L. - Appl. Radiat. Isot. 42: 173 (1991)