Journal of Sciences, Islamic Republic of Iran 15(3): 241-244 (2004)
University of Tehran, ISSN 1016-1104

Denitration of Nitroesters with Tributyltin Hydride in the Presence of Azobisisobutyronitrile (AIBN)

H. Loghmani-Khouzani[1,*] and B.T. Golding[2]

[1] *Department of Chemistry, Faculty of Sciences, University of Isfahan, Isfahan, 81746-73441, Islamic Republic of Iran*
[2] *Department of Chemistry, University of Newcastle Upon Tyne NE1 7RU, UK*

Abstract

Among the different reducing agents tributyltin hydride was found to be a powerful reducing agent for the denitration of a series of tertiary and secondary nitroesters. The organotin residues removed from the crude product using saturated potassium fluoride solution. The yield of the reactions was 62-98%.

Keywords: Denitration; Tributyltin hydride; Nitroester

Introduction

Aliphatic nitro compounds are considered to be valuable intermediates for the preparation of various biologically active molecules [1] such as alkaloids [2], steroids [3], amino acid derivatives [4,5] and enzyme inhibitors [6]. Nitro compounds with α-hydrogen also undergo the Henry [7] and Mannich [8] reactions. Nitroalkenes are also widely used for the preparation of a variety of organic compounds [9]. These compounds possess significant biological activities and are used as insecticides [10], fungicides [11], bactericides [12], rodent-repellents [13] and as Antitumor agents [14]. The utility of nitroalkenes in organic synthesis is largely due to their ease of conversion into a variety of functionalities. They are strong dienophiles in Diels-Alder reactions. Alternatively, these electrophilic alkenes readily undergo additional reactions with various nucleophiles, thus providing an array of valuable products. Due to the wide applications of nitro compounds, they are entered into the environment through various pathways. They are hazardous, are not friendly with the nature and should be removed completely from the environment; therefore, an efficient method for its removal is very important.

In this paper several possible reducing agents that have been used for the reduction of similar compounds such as sodium hydrogentelluride [15] potassium hydroxide in ethylene glycol [16], sodium salt of methanethiol [17] samarium iodide [18], trialkyl or aryl tin hydride [19], triethylsilane [20], N-benzyl-1,4-dihydronicotinamide [21], sodium hypophosphorus acids or their salts [22] and *tetrakis*(dimethyl-amino)ethylene [23], have been examined for denitration of eight tertiary and secondary esters. Among these reducing agents only tributyl tin hydride was found to be effective for this purpose.

Experimental

Materials and Methods

Chemicals were purchased primarily from Aldrich Chemical Company, and were used without further purification. Solvents were distilled from calcium hydride before use, except DMSO and DMF, which were purchased anhydrous. Petrol was the fraction boiling in the range 40-60°C.

* *E-mail: log119@sci.ui.ac.ir*

TLC was carried out using aluminium plated pre-coated with silica gel (Kieselgel 60 F_{256}, 0.2 mm, Merck).Visualization was done by UV light and $KMnO_4$.

Silica gel (flash Kiesegel 60) was used for column chromatography.

^1H and ^{13}C NMR spectra were recorded at the stated frequencies, using deuterated solvent as internal standards. 300 MHz spectra were recorded on a Bruker Avance BVT3200 spectrometer and 500 MHz spectra on a Jeol spectrometer.

Mass spectra were recorded on a Kratos MS80 RF spectrometer.

Infrared spectra were recorded on a Nicolet 20-PC Fourier transform IR spectrometer.

The starting material nitroesters were prepared are previously described [26] by condensation of appropriate nitro alkanes (Entries 4, 5, 6, 7, 8) or ethyl nitro acetate (Entries 1, 3) with ethyl acrylate and also condensation of benzyl bromide with ethyl nitro acetate for entry 2.The structures of the nitro compounds were identified by their ^1H and ^{13}C NMR spectra and their physical properties were compared with literature data except for starting material for entry 4 which was prepared as flows.

4-Nitro-4-phenyl-heptanedioic Acid Diethyl Ester

Tetraethyl ammonium bromide (1.02 mmol, 0.33 g) and DBU (14 mmol, 2.2 g) were added to a solution of phenylnitromethane (6.8 mmol, 1.0 g) in dry acetonitrile (15 ml). To this clear solution, ethyl acrylate (14 mmol, 1.43 g) was added drop wise and stirred at above room temperature (35°C) for 3 days. The acetonitrile was then removed in vacuo and the residue was dissolve in ether (75 ml). The resulting solution was washed with 10% aqueous Na_2CO_3 (2 x 40 ml) dried ($MgSO_4$). Evaporation of the solvent gives yellow oil. The resulting crude product was purified by flash chromatography eluted with ether

Mp 35°C

Yield: 2.1 g, 80 %

^1H NMR (300 MHz, $CDCl_3$): δ 7.36-7.19 (m, 5 H, Ar), 4.02 (q, 4H, J =7.14 Hz, 2 OCH_2), 2.69-2.60(m, 4H, 2 CH_2), 1.15 (t, 6H J =7.14 Hz, 2 CH_3).

^{13}C NMR (300 MHz, $CDCl_3$): δ 172.30 (C=O), 137.75 (C_1H), 129.9 (C_2H), 129.40 (C_3H), 126.02 (C_4H), 95.80 (C), 61.24 OCH_2), 31.68 (CH_2), 29.58 (CH_2), 14.49 (CH_3).

HRMS (EI) calcd for $C_{17}H_{23}O_4$: 291.364 (M^+-NO_2):, Found: 291.159.

Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.53; H, 6.87; N, 4.14 Found; C, 61.31; H, 7.20; N, 4.07

General Procedure for Denitration

All the compounds 1-8 were prepared by the following improved literature general method [27]. A mixture of nitro compound (10 mmol) and Bu_3SnH (12 mmol) and AIBN (3mmol) in cumene (1.5 ml) was heated at 80°C for 3 h. After cooling, saturated potassium fluoride solution (10 ml) and ethyl acetate (20 ml) were added and the mixture was stirred for 60 min. The organic layer was separated, dried ($MgSO_4$), and then evaporated. The pure products were obtained via chromatography on silica column eluting with different solvents as given in Table 1.

4-Cyano-2-(2-cyanoethyl) Butyric Acid Ethyl Ester (1)

Colourless liquid

BP 168-170°C (760 mmHg)

MS (EI) *m/e*: 194 (M^+, 8 %), 167 (10 %), 149 (60 %), 82 (100 %)

Anal. Calcd. for $C_{10}H_{14}N_2O_2$: C, 61.85; H, 7.21; N, 14.43.

Found; C, 61.98; H, 6.93; N, 15.27.

IR (Neat); 1728.94 (C=O), 2247.40 (CN) cm^{-1}

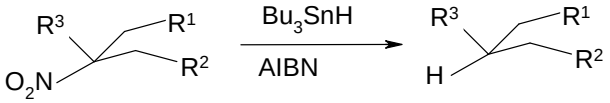
^1H NMR (500 MHz, $CDCl_3$): δ 4.15 (q, J =7 Hz, 2 H, C**H**$_2$),

2.61-2.50 (m, 1 H, C**H**), 2.50-2.31 (m, 4 H, 2 x C**H**$_2$), 2.01-1.76 (m, 4 H, 2 x C**H**$_2$), 1.22 (t, J =7 Hz, 3 H, 3 x C**H**$_3$);

^{13}C NMR (500 MHz, $CDCl_3$): δ 172.68 (**C**=O), 118.53 (**C**N), 61.25 (**C**H_2), 42.79 (**C**H), 27.24 (**C**H_2), 14.99 (**C**H_2), 13.97 (**C**H_3)

Results and Discussion

The nitro group of seven tertiary and one secondary nitroesters have been clearly replaced by hydrogen using tributyltin hydride (Bu_3SnH). Heating a mixture of nitroester (10 mmol), Bu_3SnH (12 mmol) and azobisisobutyronitrile (AIBN) (3 mmol) in cumene (1.5 mmol) at 80°C for 3 h gave the corresponding denitrated products in 62-98% yield (Table 1).



Triorganotin nitrite and the other alkoxide byproducts of these reactions were hydrolyzed slowly on silica-gel, which frequently renders purification

difficult [24,25]. In this research, organotin residues were removed from crude product by oxidative conversion to insoluble organotin fluorides using saturated potassium fluoride solution.

This reagent converts a wide variety of organotin compounds to their fluorides and greatly facilitates the purification of the crude reaction mixture. The reaction was strongly accelerated through the addition of catalytic amount of AIBN. The results strongly suggest that, the reaction proceeds via a free radical chain mechanism (Equations 1-5). In this mechanism, tributyltin radicals is added to the nitro compound to give a nitroxyl radical $Bu_3SnON(R_1R_2R_3C)O$ that, in turn, fragments to the chain-propagating alkyl radical [26]. The nitro compound (the starting material for Entry 4 of Table 1) and the Entry 1 of Table 1 were new compounds and were fully characterized. For the other Entries, their ^1H and ^{13}C NMR data are presented for the first time in Tables 2 and 3, respectively.

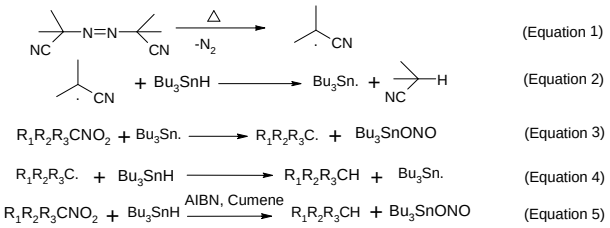


Table 1. Denitration of nitroesters

Entry	R_1	R_2	R_3	Yield	bp (°C) (mmHg)	Ref.
1	CH_2CN	CH_2CN	$CO_2C_2H_5$	98%	168-170 (760)	–
2	C_6H_5	C_6H_5	$CO_2C_2H_5$	68%	148-150 (760)	27
3	$CH_2CO_2C_2H_5$	$CH_2CO_2C_2H_5$	$CO_2C_2H_5$	95%	140-145 (1)	28
4	$CH_2CO_2C_2H_5$	$CH_2CO_2C_2H_5$	C_6H_5	78%	145-148 (6)	29
5	$CH_2CO_2C_2H_5$	$CH_2CO_2C_2H_5$	CH_3	67%	140-145 (9)	30
6	$CH_2CO_2C_2H_5$	$CH_2CO_2C_2H_5$	$(CH_2)_2CO_2C_2H_5$	90%	158-160 (0.4)	31
7	$CH_2CO_2C_2H_5$	$CH_2CO_2C_2H_5$	H	67%	266-268 (0.4)	32
8	$CH_2CO_2C_2H_5$	CH_3	CH_3	62%	Volatile substrate	33

Table 2. ^1H nmr data ($CDCl_3$ 300 MHz)

Entry	ppm
1[a]	4.15 (q, *J* =7 Hz, 2 H, C**H**$_2$), 2.61-2.50 (m, 1 H, C**H**), 2.50-2.31 (m, 4 H, 2 x C**H**$_2$), 2.01-1.76 (m, 4 H, 2 x C**H**$_2$), 1.22 (t, *J* =7 Hz, 3 H, 3 x C**H**$_3$).
2	7.21-7.00 (m, 10 H, aryl-**H**), 3.85 (q, *J* =7.14 Hz, 2 H, C**H**$_2$), 2.93-2.82 (m, 3H, C**H**$_2$ and C**H**), 2.76-2.66 (m, 2 H, C**H**$_2$), 0.91 (q, *J* =7.14 Hz, 3 H, C**H**$_3$).
3	4.15-4.02 (m, 6 H, 3 x C**H**$_2$), 2.37-2.28 (m, 1 H, C**H**), 2.27-2.15 (m, 4 H, 2 x C**H**$_2$), 1.95-1.65 (m, 4 H, 2 x C**H**$_2$), 1.25-1.10 (m, 9 H, 3 x C**H**$_3$).
4	7.30-6.98 (m, 5 H, aryl-**H**), 4.0 (q, *J* =7.09 Hz, 4 H, C**H**$_2$), 2.55-2.41 (m, 1 H, C**H**), 2.17-1.70 (m, 8 H, 4 x C**H**$_2$), 1.14 (t, *J* =7.09 Hz, 6 H, 2 x C**H**$_3$).
5	4.04 (q, *J* =7.14 Hz, 4 H, 2 x C**H**$_2$), 2.35-2.14 (m, 4 H, 2 x C**H**$_2$), 1.68-1.46 (m, 2 H, 2 x C**H**$_2$), 1.46-1.28 (m, 3 H, C**H**$_2$ and C**H**), 1.16 (t, *J* =7.14 Hz, 6 H, 2 x C**H**$_3$) 0.83 (d, *J* =5.98 Hz, 3 H, C**H**$_3$).
6	4.0 (q, *J* =7.14 Hz, 6 H, 3 x C**H**$_2$), 2.24 (t, *J* =7.80 Hz, 2 H, C**H**$_2$), 1.65-1.40 (m, 6 H, 3 x C**H**$_2$), 1.39-1.24 (m, 1 H, C**H**), 1.20 (t, *J* =7.14 Hz, 9 H, 3 x C**H**$_3$, 2 overleaped triplets).
7	4.04 (q, *J* =7.14 Hz, 4 H, 2 x C**H**$_2$), 2.24 (t, *J* =7.46 Hz, 4 H, 2 x C**H**$_2$), 1.58 (q, *J* =7.46 Hz, 4 H, 2 x C**H**$_2$), 1.48-1.35 (m, 4 H, 2 x C**H**$_2$), 1.29 (t, *J* =7.14 Hz, 6 H, 2 x C**H**$_3$).

8	4.04 (q, *J* =7.14 Hz, 4 H, 2 x C**H**$_2$), 2.22 (t, *J* =8.50 Hz, 2 H, C**H**$_2$), 1.57-1.41 (m, 3 H, C**H**$_2$ and C**H**), 1.18 (t, *J* =7.14 Hz, 3 H, C**H**$_3$), 0.82 (d, *J* =6.19 Hz, 6 H, 2 x C**H**$_3$).

[a] 500 MHz NMR

Table 3. ^{13}C nmr data ($CDCl_3$ 300 MHz)

Entry	ppm
1[a]	172.68 (**C**=O), 118.53 (**C**N), 61.25 (**C**H$_2$), 42.79 (**C**H), 27.24 (**C**H$_2$), 14.99 (**C**H$_2$), 13.97 (**C**H$_3$).
2	174.81 (**C**=O), 139.06 (**C**$_1$H, 128.85 (**C**$_2$H), 128.31 (**C**$_3$H), 126.32 (**C**$_4$H), 49.57 (**C**H), 38.22 (**C**H$_2$), 13.95 (**C**H$_3$).
3	174.69 (**C**=O), 172.69 (**C**=O), 60.38 (**C**H$_2$), 60.29 (**C**H$_2$), 43.77 (**C**H), 31.71 (**C**H$_2$), 26.93 (**C**H$_2$), 14.13 (**C**H$_3$), 14.06 (**C**H$_3$).
4	173.44 (**C**=O), 143.00 (**C**$_1$H), 128.55 (**C**$_2$H), 127.66 (**C**$_3$H), 126.56 (**C**$_4$H), 44.82 (**C**H), 32.32 (**C**H$_2$), 31.59 (**C**H$_2$), 14.14(**C**H$_3$).
5	173.44 (**C**=O), 143.00 (**C**$_1$H), 128.55 (**C**$_2$H), 127.66 (**C**$_3$H), 126.56 (**C**$_4$H), 44.82 (**C**H), 32.32 (**C**H$_2$), 31.59 (**C**H$_2$), 14.14(**C**H$_3$).
6	173.42 (**C**=O),60.20 (**C**H$_2$), 39.04 (**C**H), 31.61 (**C**H$_2$), 27.81 (**C**H$_2$), 14.08 (**C**H$_3$).
7	173.76 (**C**=O), 60.08 (**C**H$_2$), 34.04 (**C**H$_2$), 24.46 (**C**H$_2$), 24.46 (**C**H$_2$), 21.46 (**C**H$_2$), 14.17 (**C**H$_3$).
8	173.91 (**C**=O), 60.02 (**C**H$_2$), 33.67 (**C**H$_2$), 32.30 (**C**H$_2$), 27.56 (**C**H), 22.09 (**C**H$_3$), 14.10 (**C**H$_3$).

[a] 500 MHz NMR

Conclusion

Tributyltin hydride was a strong nucleophiling agent for the denitration of nitroesters, and by using the other reducing agents, in most cases all of the starting materials were recovered unchanged. However, high yields, readily conversion and good selectivity were of the noteworthy advantages of this reagent.

The effects of substituents with R_3 = H, CH_3, C_6H_5, $CH_2CH_2CO_2C_2H_5$, and $CO_2C_2H_5$ on the end of chain of substrates on denitration of nitroesters were studied and the results show that electron withdrawing groups make more stable radical intermediate so that the desired products are obtained in higher yields.

Acknowledgment

This research has been supported in part by WHO.

H. Loghmani acknowledges financial support from University of Isfahan during sabbatical leave.

Supplementary Available

^{1}H and ^{13}C NMR spectra for all nitroester and denitrated compounds (18 pages).

References

1. Node M. and Fuji K. *J. Syn. Org. Chem. Jpn.*, **48**: 389-402 (1990).
2. Jousse C. and Desmele D. *Eur. J. Org. Chem.*, **64**: 909-915 (1999).
3. Kametani T. and Nemoto H. *Tetrahedron Lett.*, **20**: 3309-3310 (1979).
4. Baldwin J.E., Haber S.B., Hoskins C., and Kruse L.I. *J. Org. Chem.*, **42**: 1239-1241 (1977).
5. Easton C.J., Roselt P. D., and Tiekink E.R. *Tetrahedron*, **51**: 7809-7822 (1995).
6. Crossley M.J., Crumbie R.L., Fung Y.M., Potter J.J., and Pegler M.A. *Tetrahedron Lett.*, **28**: 2883-2886 (1987).
7. Luzzio F.A. *Tetrahedron*, **57**: 915-945 (2001).
8. Feuer H. *The Chemistry of the Nitro Nitroso Groups*. Part 2, John Wiley & Sons, Int., pp. 117-129 (1970).
9. Kabalka G.W., Guindi H.M., and Varma R.S. Symposia, *Tetrahedron*, **46**: 7443-7447 (1990).
10. Brown A.W., Robinson D.B.W., Hurtig H., and Wenner B. *Can. J. Res.***, 26 D**: 177 (1948).
11. Brian P.W., Grove J.F., and McGrowan J.C. *Nature*, **158**: 876 (1946).
12. Schales O. and Graefe H.A. *J. Am. Chem. Soc.*, **74**: 4486 (1952).
13. Harker R.J. *U. S. Patent 2*, **889**: 246 (1959); *Chem. Abstr.*, **53**: 17414i (1959).
14. Zee-Cheng K. and Cheng C. *J. Med. Chem.*, **12**: 157 (1969).
15. Suzuki H., Takaoka K., and Osuka A. *Bull. Chem. Soc. Jpn.*, **58**: 1067-1068 (1985).
16. Lytko-Krasuska A., Piotrowska H., and Urbanski T. *Tetrahedron Lett.*, 1243-1246 (1979).
17. Kornblum N., Carlson C.S, and Smith R.G. *J. Am. Chem. Soc.*, **101**: 647 (1979).
18. Kang H.Y. and Hong W.S. *Tetrahedron Lett.*, **36**(42): 7661-7664 (1995).
19. Tormo J., Hays D.S., and Fu G.C. *J. Org. Chem.*, **63**: 5296-5297 (1998).
20. Ono N., Hashimoto T., Tue X.J., Kaji A. *Tetrahedron Lett.*, **28**: 2277 (1987).
21. Ono N., Tamura R., and Kaji A. *J. Am. Chem. Soc.*, **105**: 401-4022 (1983).
22. Jang D.O. and Cho D.H. *Tetrahedron Lett.*, **43**: 5921-5924 (2002).
23. Carpenter W. *J. Org. Chem.*, **30**: 3082-3084 (1965).
24. Sibi M.P. *J. Am. Chem. Soc.*, **118**: 3063 (1996).
25. Tanner D.D., Harrison D.J., Chen J., Kharrat A., Wayne D.D.M., Griller D., and McPhee D.J. *J.Org. Chem.*, **55**:

3321-3325 (1990).
26. Fu Y., Hammarstran L.G.J., Miller T.J., Fronczek F.R., McLaughlin M.L., and Smf Hammer R.P. *J. Org. Chem.*, **66**: 7118-7124 (2001).
27. Ono N., Miyake H., Kamimura A., Hamamoto I., Tamura R., and Kaji A. *Tetrahedron* **41**(19): 4013-4023 (1985).