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A NEW SYNTHETIC METHOD: DIRECT REPLACEMENT OF THE NITRO GROUP BY HYDROGEN OR DEUTERIUM

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Summary: The nitro group in tertiary or secondary aliphatic nitro compounds is replaced by hydrogen or deuterium on treatment with tributyltin hydride or tributyltin deuteride, respectively.

The utility of aliphatic nitro compounds is firmly established both for the manifold transformations of the functional group and for the creation of new carbon-carbon bonds under extremely mild conditions.[1] However, the synthetic application of aliphatic nitro compounds should be extended if efficient and selective methods become available for replacing the nitro group by hydrogen or deuterium.[2] We have discovered that tin hydrides or deuterides are excellent reagents for this purpose.

The nitro compounds listed in the Table were each treated under nitrogen with 1.2 equivalent of Bu_3SnX (X = H or D) in refluxing benzene in the presence of azobisisobutyronitrile (AIBN, 20 mol%) to give the reduction products listed. The reduction products are readily separated from tin compounds by passing through silica gel using hexane or benzene.[3]

$$R\text{-}NO_2 + Bu_3SnX \xrightarrow[\text{benzene, reflux}\ 1\text{-}2\ h]{\text{AIBN (20 mol\%)}} R\text{-}X\ (X = H \text{ or } D) + Bu_3SnONO$$ [3]

Thus, the nitro group in tertiary nitro compounds and some secondary nitro compounds substituted by electron accepting groups is replaced by hydrogen or deuterium in good yield. However, other secondary or primary nitro compounds are inert to the present procedure. Under the present conditions Bu_3SnH replaces the nitro group selectively by hydrogen without affecting other functionalities such as keto, ester, cyano, chloro, or organic sulfur groups as shown in the Table. Some of them are generally reduced with Bu_3SnH in the absence of the nitro group in the molecule.[4] This selectivity enhances the utility of the present reaction in organic synthesis, and the following transformations are possible. (1) The Michael addition of the aliphatic nitro compounds followed by replacement of the nitro group by hydrogen (example, entry

5, 6, 7, 8, 9, 10). (2) The nucleophilic substitution reaction via one electron transfer processes ($S_{RN}1$)[5] followed by replacement of the nitro group by hydrogen (entry 11, 12, 13). (3) Acylation[6] of aliphatic nitro compounds followed by replacement of the nitro group by hydrogen (entry 14, 15).

The high selectivity of the reduction suggests that it may involve the one electron transfer reaction from tin radical to the nitro compounds at the key steps. One possible pathway is shown here. This pathway is further confirmed by the following facts. The reaction proceeds very slowly in the absence of AIBN and it is completely inhibited by the addition of only small amounts of the strong electron acceptor such as m-dinitrobenzene.

$$Bu_3SnH + In \longrightarrow Bu_3Sn\cdot \qquad In = Me_2\dot{C}CN$$

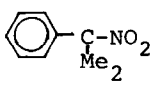
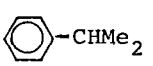
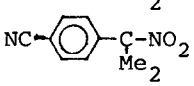
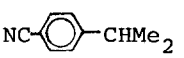
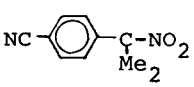
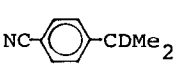
$$Bu_3Sn\cdot + R\text{-}NO_2 \longrightarrow Bu_3Sn^+ + R\text{-}NO_2^-$$

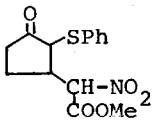
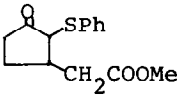
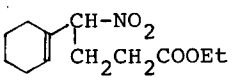
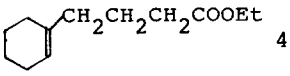
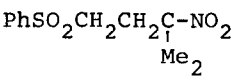
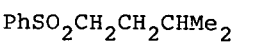
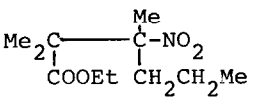
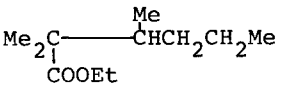
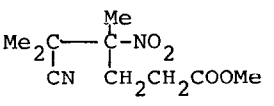
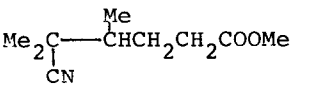
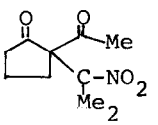
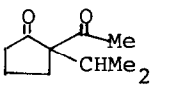
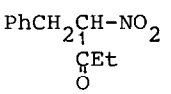
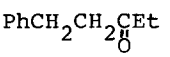
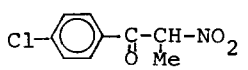
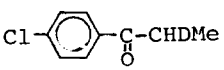
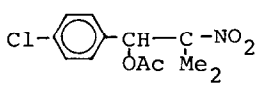
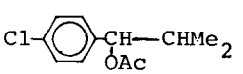
$$R\text{-}NO_2^- \longrightarrow R\cdot + NO_2^-$$

$$R\cdot + Bu_3SnH \longrightarrow R\text{-}H + Bu_3Sn\cdot$$

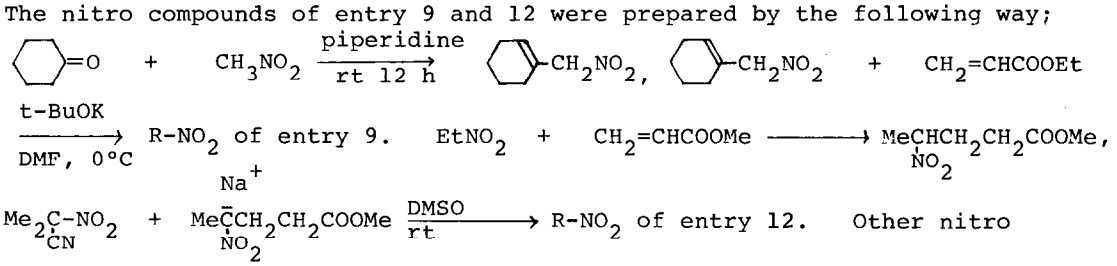
However, the formation of R· from $R\text{-}NO_2$ and $Bu_3Sn\cdot$ by one step cannot be ruled out by the present results. Synthetic applications to more functionally complex compounds and the detailed mechanism of the reaction are now under invesitigation.

Table Replacement of the Nitro Group by H or D with Bu_3SnX (X = H or D)

Entry	$R\text{-}NO_2$	Time, h	Product	Isol. Yield, %
1		1.5		92
2		1.5		94
3		1.5		85
4	$Me_3CCH_2\overset{Me}{\underset{Me}{C}}\text{-}NO_2$	2.0	$Me_3CCH_2CHMe_2$	75
5	$Me_2CHCH_2\overset{Me}{\underset{CH_2CH_2CN}{C}}\text{-}NO_2$	1.5	$Me_2CHCH_2\overset{Me}{C}HCH_2CH_2CN$	90
6	$NCCH_2CH_2\overset{Me}{\underset{CH_2CH_2CN}{C}}\text{-}NO_2$	1.5	$NCCH_2CH_2\overset{Me}{C}HCH_2CH_2CN$	92
7	$PhCH\underset{CH_2CH_2COOMe}{}\text{-}NO_2$	1.5	$PhCH_2CH_2CH_2COOMe$	64

8		1.5		75
9		1.25		48
10		1.5		91
11		1.5		77
12		2.0		89
13		1.5		60
14		1.5		78
15		1.5		78
16		1.5		83

The nitro compounds of entry 9 and 12 were prepared by the following way;



compounds are also prepared in good yields by the simple procedure (see ref).

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References and notes

1) D. Seebach, E. W. Colvin, F. Lehr and T. Weller, Chimia, 33, 1 (1979), N. Ono and A. Kaji, J. Synth. Org. Chem. Jpn., 38, 115 (1980), Houben-weyl, "Methoden der Organischen Chemie" 4 th ed., E. Muller, Ed., Vol. X, part 1, Georg Thieme Verlag, Stuttgart, 1971.

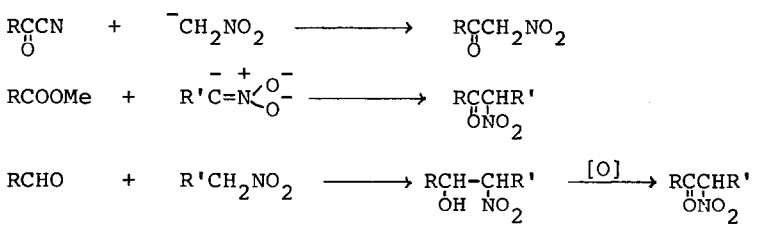
2) Three methods so far exsisted for this purpose. Method A: The use of CH_3SNa in dipolar aprotic solvents. [N. Kornblum, S. C. Carlson and R. G. Smith, J. Am. Chem. Soc., 101, 647 (1979)]. Method B: The use of KOH in ethylene glycol [A. L. Krasuska, H. Piotrowska and T. Urabanski, Tetrahedron Lett., 1243 (1979)]. Method C: The use of N-benzyl-1,4-dihydronicotinamide [N. Ono, R. Tamura and A. Kaji, J. Am. Chem. Soc., 102, 2581 (1980)]. However, these methods have severe limitations, for example, method A is not suitable for the reduction of the compounds of entry 1, 5, 6, 7, 8, 9, 10, 14, 15. In these cases nucleophilic substitution or addition by CH_3SNa may occur in preference to the reduction. Similarly, method B is not suitable for these compounds owing to its strong basicity of the reagent. The reagent of method C is not nucleophilic nor basic, but lacks reactivity. The compounds of entry 1, 2, 4, 5, 6, 7, 9, 10, 11, 12, 16 can not be reduced by this method. In these regards the method reported here is the best one known to date for replacing the nitro group by hydrogen.

3) As a tin compound $Bu_3SnOSnBu_3$ was isolated, which may be produced from Bu_3SnONO.

4) A. Hajos, "Complex Hydrides", chapter 8, Elsevier Sci., New York, 1979. M. Pereyer and J. C. Pommier, "New Applications of Organometallic Reagents in Organic Synthesis" Edited by D. Seyferth, pp 161, Elsevier Sci., New York, 1976. For the reduction of organosulfur compounds, see, C. G. Gutierrez, R. A. Stringham, T, Nitasaka and K. G. Glasscock, J. Org. Chem., 45, 3393 (1980).

5) N. Kornblum, Angew. Chem. Int. Ed., 14, 734 (1975).

6) Acylation of the nitro compounds can be done by the following reactions (see ref 1).



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