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FORMATION OF QUATERNARY CARBON CENTERS FROM TERTIARY NITRO COMPOUNDS BY FREE RADICAL METHODS

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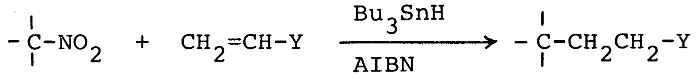
The radical intermediates generated by denitration of tertiary nitro compounds with tributyltin hydride undergo the carbon-carbon bond forming reaction with double bonds, which provides a useful method for the construction of quaternary carbon centers.

As tertiary nitro compounds are available via various routes,1) any processes which result in the replacement of the nitro group by the carbon functionality are very attractive methods for the construction of quaternary carbon centers.2) There are only limited numbers of methods for such conversions.3) In this paper we wish to report a new procedure for converting tertiary nitro compounds (1) into quaternary carbon compounds (3).



$$-\overset{|}{\underset{|}{C}}-NO_2 \quad + \quad CH_2{=}CH{-}Y \quad \xrightarrow[\text{AIBN}]{Bu_3SnH} \quad -\overset{|}{\underset{|}{C}}-CH_2CH_2-Y$$

1 2 3

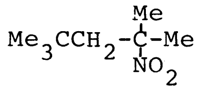
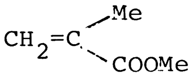
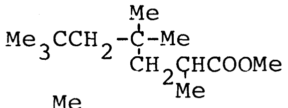
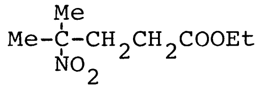
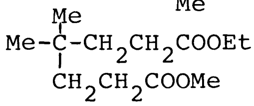
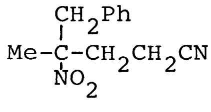
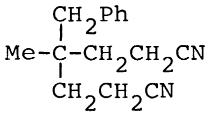
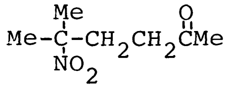
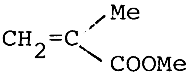
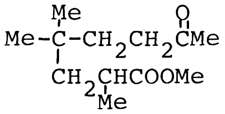
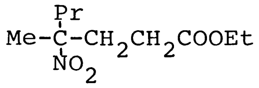
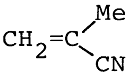
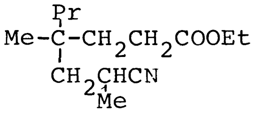
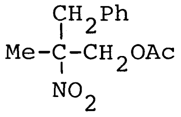
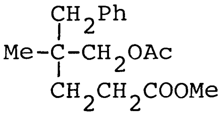
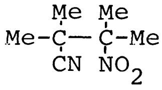
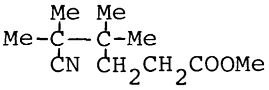
A new procedure is based on our recent findings of the replacement of the nitro group by hydrogen on treatment with tributyltin hydride4) and the carbon-carbon bond forming reactions via radical chain processes.5) Although the formation of 3 may be expected from the result reported by Giese5) (treatment of 1 with Bu_3SnH in the presence of a Michael acceptor), the yield of 3 is very low by the reaction conditions given by Giese owing to the side reactions such as telomerization of olefins (2), hydrostannation of 2, and denitrohydrogenation of 1. So the reaction conditions were modified as follows. The formation of 3 was performed by heating a mixture of 1 (4 mmol), 2 (4-5 ml), Bu_3SnH (10 mmol), and azobisisobutyronitrile (AIBN, 4 mmol) in benzene (1-3 ml) at 100 °C for 5-10 min. Pure 3 was isolated by column chromatography (silica gel/benzene-hexane) after the evaporation of olefins and the solvent.

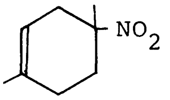
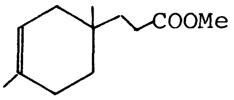
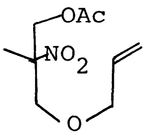
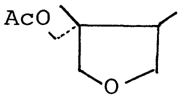
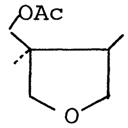
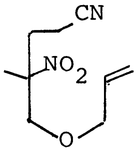
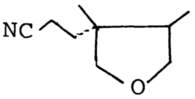
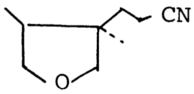
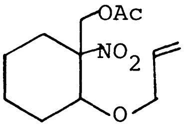
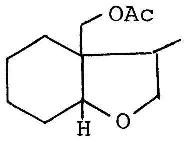
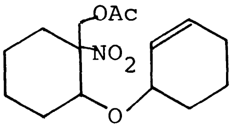
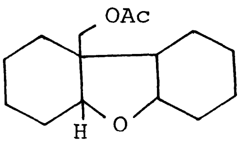
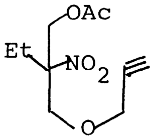
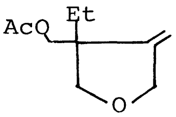
When suitably located double bonds or triple bonds are present in the nitro compounds, radical cyclization takes place to yield the exo-cyclized compounds. As intramolecular radical addition to double bonds is a facile process compared to intermolecular one, no difficulties are encountered in this case.

The cyclization was performed by heating a benzene solution (0.5 M) containing the nitro compounds, Bu_3SnH (1.3 equiv.), and AIBN (0.3 equiv.) at 80 °C for 2 h to yield the exo-cyclized products in good yield. Thus, the reaction is relatively insensitive to steric hindrance and forms a quaternary carbon center easily as in other cases of radical reactions.[1,6] The results are summarized in Table 1.

Application of radical reactions to organic synthesis has recently received much attention and various important reactions have been found in this field, where alkyl halides, selenides, sulfides, thiocarbonyl compounds, or alkylmercury salts have been used as precursors as alkyl radicals.[6] Now a new method for generation of alkyl radicals is in our hands, where aliphatic nitro compounds are used as precursors of alkyl radicals. This promises a potent utility for organic synthesis, because aliphatic nitro compounds are available by various methods. For example, the nitro compounds in Table 1 are readily prepared by the oxidation of the corresponding amines, the Michael reaction of nitro compounds, $S_{RN}1$ reaction, hydroxymethylation of nitro compounds, or the Diels-Alder reaction of nitroolefins, respectively.[1]

Table 1. Synthesis of Quaternary Carbon Compounds

Entry	$R-NO_2$	Olefins	Products, Isol. yield/%	
1	 $Me_3CCH_2-\overset{Me}{\underset{NO_2}{C}}-Me$		 $Me_3CCH_2-\overset{Me}{\underset{CH_2\underset{Me}{C}HCOOMe}{C}}-Me$	42
2	 $Me-\overset{Me}{\underset{NO_2}{C}}-CH_2CH_2COOEt$	$CH_2=CH-COOMe$	 $Me-\overset{Me}{\underset{CH_2CH_2COOMe}{C}}-CH_2CH_2COOEt$	60
3	 $Me-\overset{CH_2Ph}{\underset{NO_2}{C}}-CH_2CH_2CN$	$CH_2=CH-CN$	 $Me-\overset{CH_2Ph}{\underset{CH_2CH_2CN}{C}}-CH_2CH_2CN$	44
4	 $Me-\overset{Me}{\underset{NO_2}{C}}-CH_2CH_2\overset{O}{\overset{\|}{C}}Me$		 $Me-\overset{Me}{\underset{CH_2\underset{Me}{C}HCOOMe}{C}}-CH_2CH_2\overset{O}{\overset{\|}{C}}Me$	62
5	 $Me-\overset{Pr}{\underset{NO_2}{C}}-CH_2CH_2COOEt$		 $Me-\overset{Pr}{\underset{CH_2\underset{Me}{C}HCN}{C}}-CH_2CH_2COOEt$	58
6	 $Me-\overset{CH_2Ph}{\underset{NO_2}{C}}-CH_2OAc$	$CH_2=CH-COOMe$	 $Me-\overset{CH_2Ph}{\underset{CH_2CH_2COOMe}{C}}-CH_2OAc$	40
7	 $Me-\underset{CN}{\overset{Me}{C}}-\underset{NO_2}{\overset{Me}{C}}-Me$	$CH_2=CH-COOMe$	 $Me-\underset{CN}{\overset{Me}{C}}-\underset{CH_2CH_2COOMe}{\overset{Me}{C}}-Me$	36

8		CH$_2$=CH-COOMe		45
9			 +  7) 65 : 35	90
10			 +  8) 70 : 30	85
11			 two isomers of a ratio of 85 : 15 9)	74
12			 two isomers of a ratio of 65 : 35 10)	67
13				78

All products were identified by IR, NMR, and mass spectra. The isomer ratio of entries 9, 10, 11, and 12 was determined by GLC and NMR. The structure of them was tentatively assigned as those in this table by the chemical shift of the methyl groups. As steric factors play an important role in the radical cyclization,[11] bulky groups are probably located at the trans position each other. In the case of entries of 11 and 12, the formation of the cis-fused bicyclic compound is favored over that of the trans compounds, which is demonstrated in many radical cyclization reactions.[12]

References

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7) The major isomer: NMR ($CDCl_3$) δ 0.94 (3H, d), 0.96 (3H, s), 1.9-2.1 (1H, m), 2.05 (3H, s), 3.4-4.2 (6H, m). The minor isomer: NMR ($CDCl_3$) δ 0.92 (3H, d), 1.06 (3H, s), 1.9-2.2 (1H, m), 2.05 (3H, s), 3.4-4.2 (6H, m).

8) The major isomer: NMR ($CDCl_3$) δ 0.94 (3H, d), 0.96 (3H, s), 1.8-2.2 (3H, m), 2.3-2.5 (2H, m), 3.4-4.2 (4H, m). The minor isomer: NMR ($CDCl_3$) δ 0.92 (3H, d), 1.04 (3H, s), 1.8-2.2 (3H, m), 2.3-2.5 (2H, m), 3.4-4.2 (4H, m).

9) The major isomer: NMR ($CDCl_3$) δ 1.02 (3H, d), 1.2-2.2 (9H, m), 2.10 (3H, s), 3.54 (1H, m), 3.8-4.4 (4H, m). The minor isomer: NMR ($CDCl_3$) δ 0.92 (3H, d), 1.2-2.2 (9H, m), 2.10 (3H, s), 3.54 (1H, m), 3.8-4.4 (4H, m).

10) The major isomer: NMR ($CDCl_3$) δ 1.2-2.7 (17H, m), 2.04 (3H, s), 3.58 (1H, m), 3.98 (1H, m), 4.02 (2H, d). The minor isomer: NMR ($CDCl_3$) δ 1.2-2.0 (17H, m), 2.04 (3H, s), 4.0 (1H, m), 4.26 (1H, d), 4.40 (2H, m).

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