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A NEW METHOD FOR REGIOSELECTIVE α-MONO- OR α,α-DI-DEUTERATION OF CARBONYL COMPOUNDS

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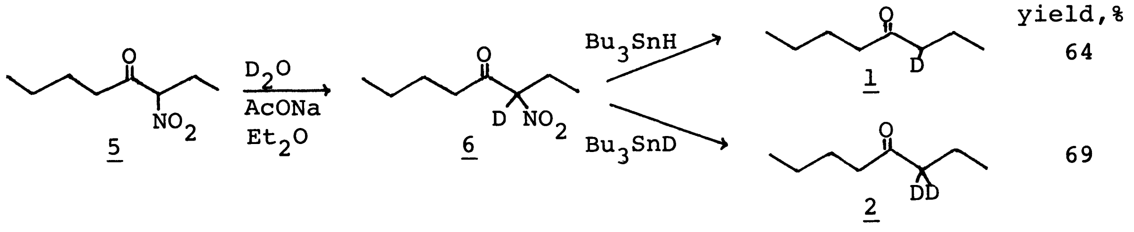
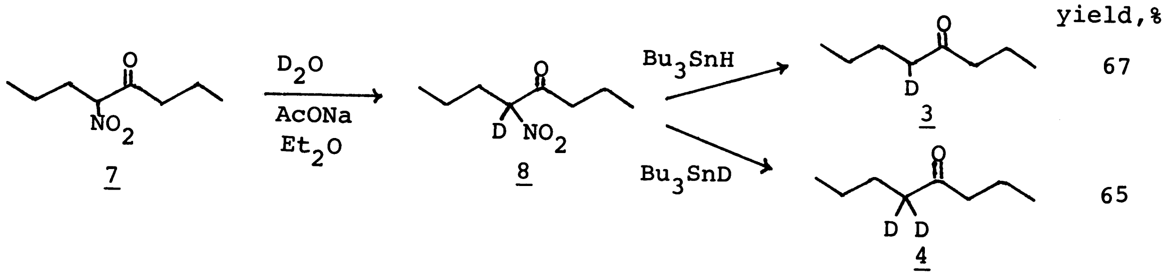
Mono- or di-deuterated carbonyl compounds are prepared regioselectively by the base-catalyzed H-D exchange of α-hydrogen of aliphatic nitro compounds and the subsequent replacement of the nitro group by H or D with Bu_3SnX (X = H, D).

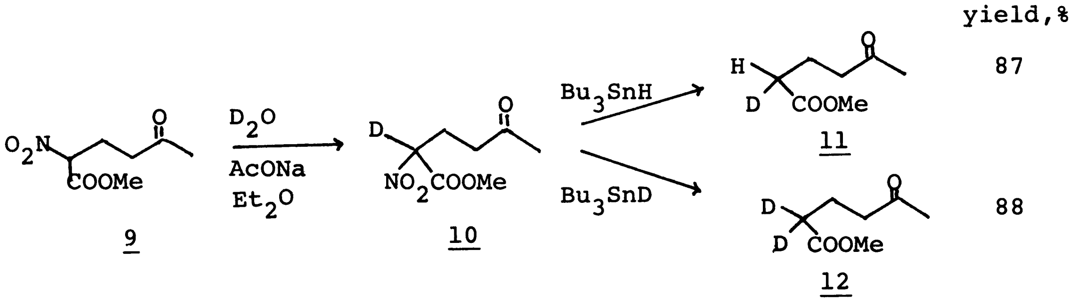
It is not easy to prepare mono- or di-deuterated carbonyl compounds regioselectively. For example, α-deuteration of 4-octanone by base catalysis gives a complex mixture of 3-D_1(1), 3-D_2(2), 5-D_1(3), 5-D_2(4), and others, and it is very difficult to prepare each of them selectively. In this paper we report a simple successful method for this conversion, which is based on our recent findings of replacement of a nitro group by H or D with Bu_3SnX (X = H, D).1)

α-Nitroketones can be prepared regioselectively by acylation of nitroparaffins2) or nitration of enol acetates.3) For example, 3-nitro-4-octanone (5) or 5-nitro-4-octanone (7) was prepared from 1-nitropropane and pentanal or from 1-nitrobutane and butanal, respectively, by the oxidation of the corresponding β-nitro alcohols. Then α-nitroketones were treated with D_2O-AcONa in diethyl ether to result in the clean H-D exchange giving 6 or 8, respectively. The ratio of exchange was estimated to be more than 95% by ^1H NMR. The choice of bases and solvents is important for this exchange. More stronger bases than AcONa may cause the side reactions. In general, α-nitroketones are labile to basic conditions.4) The exchange proceeded at a reasonable rate in diethyl ether, but it was very slow in other solvents such as benzene or acetonitrile. Treatment of 6 or 8 with Bu_3SnX (X = H, D) gave 1, 2, 3, or 4, respectively, in good yields. The D content of the product was very high, which depended on only the first exchange step.





Another important merit of using nitro compounds is that α-hydrogen of the nitro function is more readily exchanged with D than other acidic hydrogens. For example, compound 9 gave 10 selectively by treatment eith D_2O-AcONa in diethyl ether, although 9 had six acidic hydrogens. Compounds 11 and 12, mono- and di-deuterated at α-position of the methoxycarbonyl group, respectively, were obtained selectively from 10 without any contamination of D at α-position of the carbonyl group.



Typical procedure: A mixture of 9 (1.42 g, 7.5 mmol), D_2O (1.1 ml), AcONa (0.57 g, 7.0 mmol), Et_2O (15 ml) was stirred at room temperature for 5 h. The ether layer was dried and concentrated. The same procedure was repeated once more to give 10 (1.35 g, 95%). NMR (CCl_4) δ 2.2 (s, 3H), 2.3 (t, 2H), 2.4 (t, 2H), 3.8 (s, 3H); the peak at δ 5.1 due to α-proton of the nitro group completely disappeared. Then a mixture of 10 (0.540 g, 2.84 mmol), Bu_3SnD (1.08 g, 3.69 mmol), AIBN (0.14 g, 0.85 mmol) in benzene (10 ml) was refluxed for 2 h. Column chromatography (silica gel, benzene-hexane) gave pure 12 (0.36 g, 88%). NMR (CCl_4) δ 0.9 (t, 2H), 2.05 (s, 3H), 2.45 (t, 2H), 3.60 (s, 3H). Similarly 11 was obtained by using Bu_3SnH. NMR (CCl_4) δ 0.9 (q, 2H), 2.05 (s, 3H), 2.30 (t, 1H), 2.45 (t, 2H), 3.60 (s, 3H).

References

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(3) P. Dampawan and W. W. Zajac, Jr., Tetrahedron Lett., 135 (1982), and references therein. Review of cyclic α-nitroketones, see: R. H. Fischer and H. M. Weitz, Synthesis, 261 (1980).

(4) Ring cleavage of cyclic α-nitroketones under basic conditions is popular, so similar reaction may occur in the acyclic case. (see ref 3).

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