SYNLETT
Spotlight 451

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research.

N,N-Dimethylaniline (NNDMA)
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Introduction

N,N-Dimethylaniline (NNDMA, CAS: 121-69-7, Scheme 1) is a colorless liquid with a boiling point of 193–194 °C. It is a simple but widely applied reagent. It is not only used as a starting material in the synthesis of dyestuffs, pharmaceuticals, agrochemicals, and fine chemicals, but also used as a solvent, stabilizer, and analytical reagent. The low price of NNDMA (due to the industrial production) has played an important role for its applications.

Scheme 1

Abstracts

(A) Activation of C–H Bond in N–Me:
Using metal catalysts and oxidants, the C–H bond of the N–Me group of NNDMA can be activated and replaced by an unsaturated compound like an alkene,2 alkynyl,3 CN,4,5 C=N,6 and active methylene.5,7 There are two N–Me groups on NNDMA, but a single C–H bond activation is much easier. With the above reaction, the intermediate compounds are obtained in high yield under mild conditions. Iron(II), copper(I), ruthenium, and iridium metal salts are usually used as the catalysts, and tert-butyl hydroperoxide (TBHP) or O2 is used as the oxidant. The C–H bond in N–Me is activated, and the hydrogen atom can be replaced by peroxide, alcohol8 and phosphoric acid ester groups.9

(B) Activation of N–C Bond in N–Me:
By C–N bond cleavage, amide, N-nitrosamines and other nitrogen-containing compounds can be prepared under mild conditions in high yield. The methyl group can be replaced by an acetyl group with FeCl2 and tert-butyl hydroperoxide,10 and it can be replaced by NO with o-iodoxybenzoic acid (IBX), nitromethane, and R4NX (X = halide).11 With diazoacetate and FeCl3, the methyl group can be replaced by an acetate group.12 Cytochrome P450 enzymes can achieve demethylation of NNDMA.13

SYNLETT 2013, 24, 2616–2617
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(C) Cyclization Reactions:
Tetrahydroquinolines can be prepared using Ru(bpy)₃Cl₂ or CuBr as the catalyst and air or TBHP as the terminal oxidant.¹⁴⁻¹⁶ But, to the best of our knowledge, all products obtained are racemates.

![Cyclization Reaction Diagram]

(D) Donation of a One-Carbon Unit:
NNDMA can donate a one-carbon unit after catalysis and oxidation with iron. The reaction can be used to prepare bis-1,3-dicarbonyl derivatives.¹⁷ NNDMA was also a carbonyl source in the mild and selective ruthenium-catalyzed formylation of indoles.¹⁸

![Donation of One-Carbon Unit Diagram]

(E) Substitutions on the Benzene Ring:
Regioselective reactions of NNDMA in the ortho, meta, and para positions on the benzene ring can be realized. The regioselective, catalyzed cross-dehydrogenative coupling (CDC) usually proceeds on the ortho or para position of the benzene ring.¹⁹ and sulfurochloric acid can react with the meta position to prepare 4'-substituted compounds having 5-HT₆ receptor affinity.²⁰ In addition, the benzene ring of NNDMA can be reduced by NHCl-stabilized ruthenium derivatives.²¹ NNDMA can donate a one-carbon unit after catalysis and oxidation with iron. The reaction can be used to prepare bis-1,3-dicarbonyl derivatives.²²

![Substitutions on Benzene Ring Diagram]

(F) Other Special Uses:
Used as solvent or reaction additive, NNDMA can stimulate the enantioselectivity Friedel–Crafts alkylation of furans and indoles.²³ Moreover, it can donate NMe₂ groups²⁴ and promote ortho lithiation of anilines by formation of quaternary ammonium salts.²⁵

References