Chemoselective Reduction of Nitrobenzylidene Malonic Diester by an NADH Model

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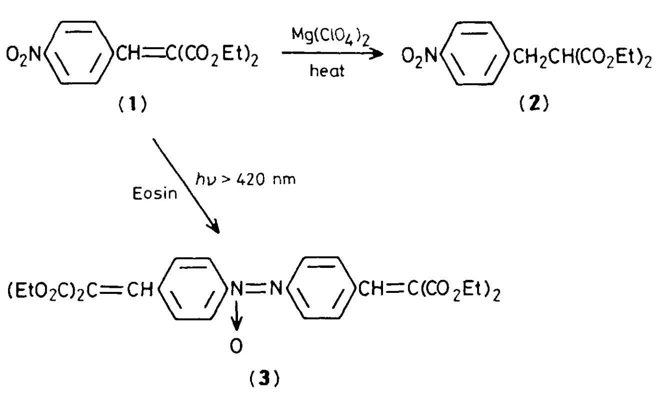
The carbon–carbon double bond or the nitro group of nitrobenzylidene malonic diethyl ester has been reduced selectively with Hantzsch ester using a metal ion catalyst or by sensitized photoirradiation, providing evidence of a one step hydride transfer and/or multistep hydrogen transfer mechanism respectively.

The mechanism by which NADH transfers hydrogen in redox reactions has been extensively examined in model systems. Controversy remains on whether the process occurs by a one step hydride transfer or by a multi-step electron–proton–electron transfer mechanism.[1] Recently, Pandit[2] reported observations of specificity in the reduction of carbon–carbon double bonds in α-keto-β,γ-unsaturated esters by NADH models that are consistent with a hydride transfer mechanism. The results of Kreevoy[6] on measuring the rate and equilibrium constants of hydride transfer reactions also eliminated the possibility of a multistep mechanism. It occurred to us that more evidence could be obtained by employing different methods of reduction, say, by metal ion catalysis or photosensitization, using an NADH model so that either the carbon–carbon double bond or the nitro group in nitrobenzylidene malonic diester is reduced selectively.

A mixture of 4-nitrobenzylidene malonic diethyl ester (**1**) (NME, 0.125 M), Hantzsch ester (HE, 0.15 M), and $Mg(ClO_4)_2$ (0.125 M) in 80 ml 9 : 1 acetonitrile–methanol was refluxed for 6.5 h. The product was isolated by column chromatography on silica gel giving 4-nitrobenzyl malonic diethyl ester (**2**). ^1H N.m.r. analysis of the reduced compound showed doublet



peaks at *ca.* δ 3.3 which are characteristic of the α-methylene groups in the product [yield 96.7%; m.p. 59 °C (from EtOH), (lit.,[3] 63 °C)].

Also, a mixture of 9 : 1 pyridine–methanol solution containing HE (2×10^{-2} M), eosin (5×10^{-5} M), and NME (5×10^{-3} M) was irradiated under argon by a 450 W sodium lamp at >420 nm for 1 h. The ester (**3**) (m.p. 110 °C) was isolated by t.l.c. as orange crystals. The structure of the compound was confirmed by spectroscopic analysis. ^{1}H N.m.r. spectroscopy indicated that the carbon–carbon double bond remained unaltered [$\lambda_{max.}$ (EtOH) 358 nm (ε 33 000 l mol^{-1} cm^{-1}); $\nu_{max.}$ (KBr) 1732 and 1711 (CO), 1260 [–N(O)=N–], 1220 and 1200 (C–O–C) cm^{-1}; *m/z* 538 (M^+)]. It is likely that the azoxy compound (**3**) is formed from the condensation of the primary photoreduction product, the hydroxylamine *p*-$HONHC_6H_4CH{=}C(CO_2Et)_2$, and the nitroso compound *p*-$ONC_6H_4CH{=}C(CO_2Et)_2$ during subsequent separation processes.

The effect of anthracene as a diffusion-controlled quencher of the photoreaction suggests that both an excited triplet state and an unquenchable excited singlet state of eosin participate in the photoreaction as reported previously.[4] From the Stern–Volmer plot of quantum yield *vs.* anthracene concentration, the triplet reaction rate constant has been calculated to be 7.3×10^6 l mol^{-1} s^{-1}. It was found that the fluorescence of eosin was quenched by both NME and HE. The quenching rate constant k_q in 9 : 1 pyridine–methanol (7.9×10^9, 1.4×10^9 l mol^{-1} s^{-1} respectively) approximates to a value predicted for electron transfer quenching of excited eosin by NME and HE (7.3×10^9, 7.3×10^9 l mol^{-1} s^{-1} respectively).

After flash photolysis of a mixture of HE (5×10^{-5} M), eosin (5×10^{-5} M), and NME (5×10^{-3} M) in 9 : 1 pyridine–methanol, the transient spectra 20 ns to 250 μs after the excitation flash showed a maximum at 466 nm due to the eosin cation radical[5] (*t* 7.1 μs, k_d 1.4×10^5 s^{-1}), demonstrating that one-electron transfer from eosin to NME is responsible for the initial process.

It is of mechanistic interest to note that photosensitized reduction of 4-nitrobenzylidene malonic diethyl ester has no parallel with the reaction in the dark. For the photosensitized reaction, a mechanism involving sequential electron–proton–electron transfer is consistent with formation of the azoxy compound. In contrast, a direct hydride transfer mechanism would give the product with the reduced carbon–carbon double bond by a metal ion catalysed dark reaction.

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