Efficient Photo-induced Electron Transfer Methodology for Dual Epimerization of Diels–Alder *endo* Adducts to *exo* Isomers

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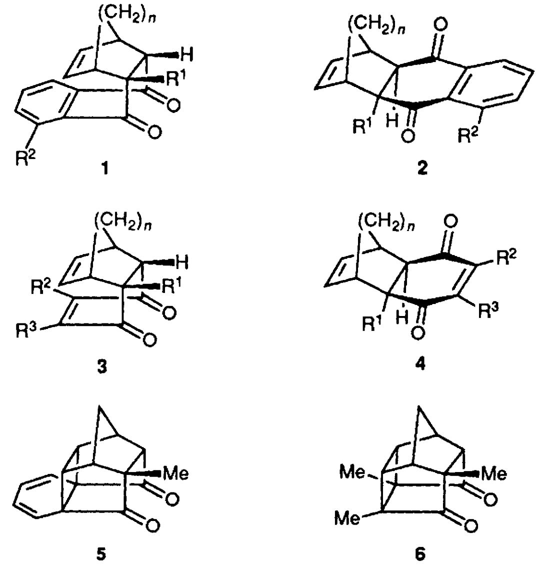
Irradiation of Diels–Alder *endo* adducts with triethylamine in ethanol at 300 nm furnishes high yields (>90%) of the corresponding *exo*-isomers.

The Diels–Alder (D–A) reaction,[1] with its intramolecular,[2] asymmetric,[3] hetero-[4] and inverse-electron-demand[5] variants, is a synthetically highly useful reaction.[6] However, predominant *endo*-selectivity usually associated with D–A reactions limits its applicability, especially for those targets which demand *exo*-selectivity.[7] Recently there have been some attempts to alter the *endo*-selectivity in a D–A reaction by interfering with either reaction conditions,[8] or transition state[9] or modifying substrates.[10] A recent theoretical study highlights the complexity of problems even for unicentre *endo*–*exo* epimerization.[11] Since *exo*-isomers are thermodynamically favoured, the major product at elevated temperatures might be expected to be the *exo*-isomer formed *via* a fast equilibrating retrodiene mechanism, but this expectation is not borne out in practice.[12] We report a mild, highly efficient, synthetically useful, one-pot procedure for *endo* to *exo* isomerization with a readily available reagent.

The various D–A *endo*-cycloadducts, *e.g.* **1a–f** and **3a–e**, used in our studies were prepared by heating either cyclopentadiene or cyclohexa-1,3-diene with appropriate dienophiles, using standard procedures (Scheme 1; Table 1).[6,7] As illustrated, the photochemical dual epimerization to *exo*-products **2a–f** (except **2d**) and **4a–e** (except **4c**) was highly efficient (>90% isolated yield) in terms of substrate consumption and product formation.† Loss of bromine was observed with **3d** during *endo* to *exo* isomerization. For substrates with a methyl group α to the carbonyl, *e.g.* **1d** and **3c**, the corresponding cage compounds **5** (22%)† and **6** (30%)† were formed during extended irradiation.



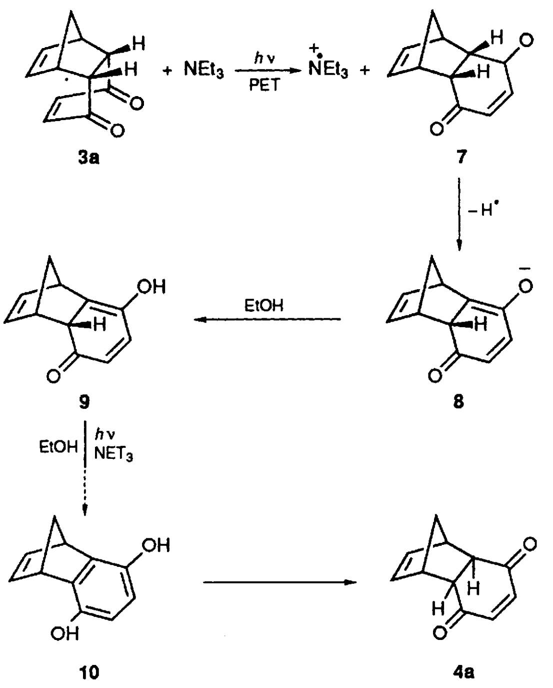
Scheme 1 *Conditions*: TEA, EtOH, *hν*, for **1** → **2**, **3** → **4**

In a typical experiment, a degassed solution of ethanol containing the appropriate *endo* compound (0.02–0.05 mol dm^{-3}) and triethylamine (TEA, 10–20% of volume of ethanol) in a Pyrex vessel was irradiated for 2–6 h at 300 nm in a Rayonet–Srinivasan photochemical reactor. Reactions were monitored by GLC and/or TLC. Normally no *endo* compounds were detectable after irradiation. After removal of ethanol by rotary evaporation, the *exo*-products were isolated either by removing TEA *in vacuo* or by extraction after treating the reaction mixture with 10% HCl. The products were purified by filtering through a small silica gel column and

Table 1 Epimerization of Diels–Alder adducts **1** and **3**

n	R^1	R^2	R^3	Substrate	Product	Yield (%)
1	H	H	—	**1a**	**2a**	96
1	H	OH	—	**1b**	**2b**	92
1	H	OMe	—	**1c**	**2c**	94
1	Me	H	—	**1d**	**5**[a]	22
2	H	H	—	**1e**	**2e**	91
2	H	OH	—	**1f**	**2f**	90
1	H	H	H	**3a**	**4a**	95
1	H	H	Me	**3b**	**4b**	92
1	Me	Me	Me	**3c**	**6**[b]	30
1	Br	H	H	**3d**	**4a**	90
2	H	H	H	**3e**	**4e**	92

[a] **2d** was not detected. [b] **4c** was not detected.



Scheme 2

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† All *exo*-compounds exhibited satisfactory IR, ^{1}H NMR, ^{13}C NMR and mass spectra. Where possible, authentic samples of *exo*-isomers were prepared by carrying out large scale D–A reactions and isolating the minor *exo*-isomer.

subsequent recrystallization or bulb-to-bulb distillation. Use of other photochemical electron donors,[13] *e.g.* HMPA (hexamethylphosphoric triamide) and DABCO (1,4-diazabicyclo[2.2.2.]octane) did not improve yields or the cleanliness of the transformations.

As control experiments, attempted reactions of **1a** and **3a** in the dark did not lead to dual epimerization. Photolysis in ethanol in the absence of TEA did not provide *exo* compounds,[14] nor did photolysis in TEA alone. Ethanol could not be replaced by benzene as solvent. Thus, irradiation, TEA, ethanol and to some extent degassing are essential.

All these results clearly point to the possibility of a photoinduced electron transfer (PET) type mechanism.[15] A plausible mechanism[15] is shown in Scheme 2. After initial excitation and inter-system crossing (ISC) of **3a**, electron transfer from TEA to triplet **3a** can give the radical anion **7** which by the loss of hydrogen atom leads to **8** or its protonated form **9**. Subsequent photoinduced second electron transfer to **8** or **9** would lead to **10** which in turn could tautomerize to thermodynamically stable *exo* **4a**. For those substrates containing methyl α to carbonyl *e.g.* **1d** and **3c**, the loss of the methyl radical from the corresponding radical ion may not be efficient, thereby hindering the *endo* to *exo* epimerization. This mechanism explains the role of the polar protic solvent as ethanol stabilizes the radical cation and radical anions and finally intercepts the anion **8**.

We recently reported *endo–exo* dual epimerization occurring *via* sequential α-cleavage and epimerization,[16] and such a change could take place in the present examples *via* β-cleavage and subsequent bond reorganisation followed by hydrogen shift. However, such mechanisms are unlikely in the presence of TEA.

We thank the Department of Science and Technology, Government of India, for partial support for instrumentation: the CSIR and UGC for fellowships (P.V.D., A.A.A., B.G.P. and P.P.K.); Dr R. A. Mashelkar, Director, NCL, for encouragement and support through a 'Kite Flying Grant' (to B.P.) and Dr P. R. Rajamohanan for NMR support with a Bruker MSL-300 SC-FT NMR spectrometer. This is NCL communication No. 4879. We thank Professor Dr K. Schaffner, Mülheim, FRG for the β-cleavage and subsequent bond reorganisation suggestion.

Received, 10th April 1990; Com. 0/01628D

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