CHEMISTRY LETTERS, pp. 1173−1176, 1991. © 1991 The Chemical Society of Japan

A Remarkably Efficient Photochemical Methodology for Endo to Exo Isomerization of Diels-Alder Cycloadducts(1)

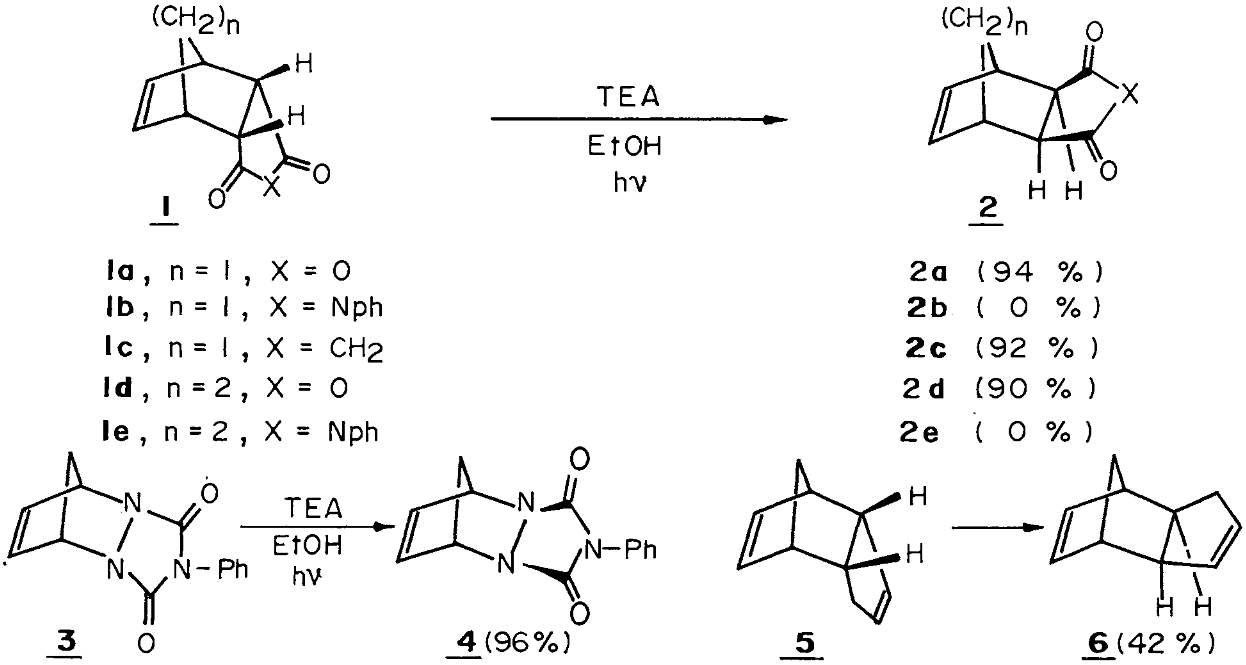
Bipin PANDEY,* Asawari A. ATHAWALE, Ravinder S. REDDY,
Pramod V. DALVI, and Pradeep KUMAR*(2)
National Chemical Laboratory, Pune 411008, India

Irradiation of a solution of ethanol containing Diels-Alder cycloadducts and 10-20% (by volume) triethylamine at 300 nm furnishes quantitative yield (>90%) of corresponding exo isomers. A probable mechanism based on photo-induced electron transfer (PET) has been described.

The last two decades have witnessed a tremendous upsurge of interest in the development of methodologies based on photo-induced electron transfer (PET) reactions.(3) 'Unprecedented', 'unusual', 'novel', 'mechanistically interesting', and 'synthetically useful' are some of the common characteristics routinely associated with these discoveries. Recently in connection with an entirely different ongoing research programme,(4) we observed endo to exo dual epimerization as a side reaction, during photolysis in alcoholic solvents.(5) One of the mechanisms proposed for this unusual behaviour was photo-enolization. We argued that if photo-enolization is the probable pathway for dual epimerization, then it should be accelerated under photo-induced electron transfer conditions, as the radical anion formed would trigger enolization.(6) This communication verifies our presumption and as a result, reports a mild, highly efficient, synthetically useful, one pot procedure for dual and unicentre epimerization of Diels-Alder (D-A) cycloadducts under photo-induced electron transfer conditions, with readily available reagents.

The various D-A cycloadducts(7) examined under PET-reaction conditions are shown in Scheme 1. As illustrated, all the endo adducts, except **1b** and **1e** (X=NPh), provided synthetically useful yields of exo products.(8,9) The dual nitrogen inversion in the transformation of **3** to **4** and cyclopentadiene dimer endo **5** to exo **6** is indeed interesting. Since exo-isomers are known to be thermodynamically favoured, one is tempted to presume that at elevated temperatures, the major product will be exo via a fast equilibrating retro-diene mechanism. However, Weisz et al.(10) experienced considerable difficulty in isomerizing **1d** to **2d** and have reported a multistep strategy. In this connection our methodology for **1d** to **2d** (90%) is noteworthy. In a typical experiment, a degassed solution of ethanol containing the appropriate endo compound (0.02-0.05 M) and triethylamine (TEA, 10-20% of ethanol by volume) in a pyrex vessel was irradiated for 2-6 hours at 300 nm in a Rayonet-Srinivasan photochemical reactor. The progress of the reaction was monitored by GLC and/or TLC. Normally no endo compounds were visible after irradiation, except in **5** to **6** where 42% yield of **6** refers to photostationary state mixture.

After removal of ethanol at rotavapor, exo products were isolated by removing TEA in vacuum. Purification of the products was accomplished usually by filtering through a small silica-gel column and subsequent recrystallization. With a view to optimizing the yield of exo products, variation of TEA concentrations, e.g. 5%, 10%, 20%, 30%, and 50% (by volume) was examined.[11] Use of other photochemical electron donors[3,12] e.g. HMPA, DABCO, and 1,4,5,8-tetramethoxynaphthalene was not encouraging in terms of yield and cleanliness of transformations.

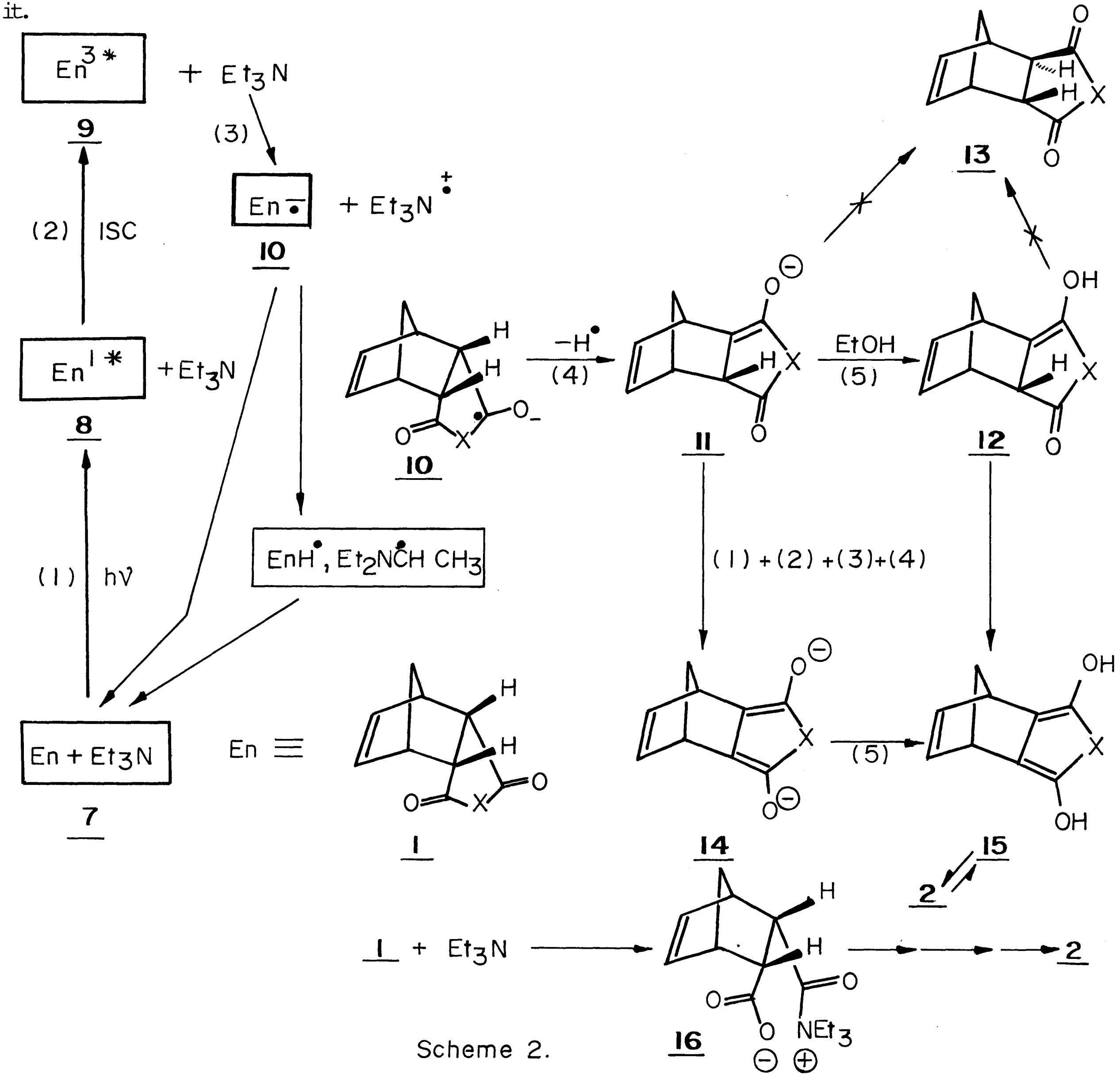


Scheme 1.

As a control experiment with **1a** and **1c** it was observed that the absence of photolysis, i.e. keeping the reaction mixture in the dark, leads to no dual epimerization (endo → exo). Neat photolysis in ethanol (i.e. without TEA) does not provide exo compounds.[5] Photolysing only in TEA was also not successful. Replacing ethanol by benzene was a failure. Thus, photolysis, TEA, ethanol, and to some extent, degassing is a must for the success of the reaction. Replacing endo compounds by maleic anhydride under successful experimental conditions does not lead to any new product formation.

All these results clearly point to the possibility of PET type mechanism.[3] The probable mechanism has been proposed for one of the endo products **1**, in Scheme 2, as per the standard norms of PET-mechanism.[3] As shown, after initial excitation and inter-system crossing (ISC) of **1**, the electron transfer from TEA to triplet En* gives the radical anion **10**, which, by the loss of hydrogen atom leads to **11** or its protonated form **12**. The formation of trans-junctured **13** from **11** or **12** is quite unlikely, due to excessive strain in the system. Subsequently photoinduced second electron transfer to **11** or **12** would lead to **14** or **15** respectively, which in turn could tautomerize to thermodynamically stable exo-**2**. Alternatively one can propose the opening of anhydride in **1a** and **1d** via **16** and subsequent stepwise unicentre epimerization to give corresponding exo products (**2a** and **2d**). However, stability of maleic anhydride and photo-products

2a and **2d** towards these reagents under photolytic conditions rules out such a possibility.[13)]Thus, there was no ethanolysis of the anhydride group. The transformation of **5** to **6** under our photolytic conditions is indeed unique and we do not have any reasonable explanations for it.



Scheme 2.

In summary, an efficient methodology for quantitative conversion of D-A endo cycloadducts to exo isomers is described and some of the possible mechanisms discussed. Mention must be made here regarding the predominant endo-selective nature of synthetically useful D-A reaction[14)]and a great need to devise either exo-selective D-A reaction[15)]or develop methodologies for endo to exo conversion.

We thank the Department of Science & Technology, Government of India, for partial support for instrumentation, the CSIR and UGC for fellowships (AAA, RSR, PVD) and Dr. R.A. Mashelkar, Director, National Chemical Laboratory, Pune, for encouragement and support (through a 'Kite-Flying' grant to BP).

References

1) NCL Communication No. 4880.

2) Dedicated to Dr. N.R. Ayyangar on the occasion of his 60th birthday.

3) Reviews: P.S. Mariano, "Synthetic Organic Photochemistry," ed by W.M. Harspool, Plenum, London(1983), p.145; J. Mattay, Angew. Chem., Int. Ed. Engl., **26**, 825(1987); J. Mattay, Synthesis, **1989**, 233; N.L. Bauld, Tetrahedron, **45**, 5307(1989).

4) B. Pandey and P.V. Dalvi, J. Org. Chem., **54**, 2968(1989); B. Pandey, U.R. Zope, and N.R. Ayyangar, Synth. Commun., **19**, 585(1989); N.N. Dhaneshwar, S.S. Tavale, T.N. Guru Row, U.R. Zope, B. Pandey, and N.R. Ayyangar, Acta Crystallogr., Sect. C, **44**, 2191(1988).

5) B. Pandey, U.R. Zope, and N.R. Ayyangar, J. Chem. Soc., Chem. Commun., **1990**, 107.

6) P.G. Sammes, Tetrahedron, **32**, 405(1976) and references therein.

7) The D-A endo cycloadducts, **1a-e**, **3**,**5** and **7** were prepared as per literature procedure. Reviews: J.G. Martin and R.K. Hills, Chem. Rev., **61**, 537(1961); J. Sauer, Angew. Chem., Int. Ed. Engl., **5**, 211(1966); J. Sauer, ibid., **6**, 16(1967).

8) We fail to understand the difference in reactivity between **1a** vs. **1b** and **1d** vs. **1e**. Perhaps the radical anion of **1b** and **1e** is highly stable due to extensive delocalization in the phenyl ring of NPh. However, this concept fails to explain the easy dual epimerization of **5** to **6**.

9) All the new exo compounds gave satisfactory IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectral data.

10) A. Weisz and A. Mandelbaum, J. Org. Chem., **53**, 5812(1988).

11) Although many variations in the experimental conditions, e.g. endo concentration, varying amine concentrations, use of other polar protic solvents, irradiation wavelengths and methodologies for isolating products are possible, our reaction conditions provided fairly satisfactory yields of exo compounds.

12) J. Cossy, J.P. Pete, and C. Portella, Tetrahedron Lett., **30**, 7361(1989) and references therein.

13) Alternatively, a recent communication from our group(5) describes the endo-exo dual epimerization via. sequential α-cleavage and epimerization. One could also visualize such a change via. β-cleavage and subsequent bond reorganization followed by hydrogen shift.

14) For intramolecular,a) asymmetric,b) hetero,c) and inverse-electron demand(d) variants of D-A reaction see: a) D. Craig, Chem. Soc. Rev., **16**, 187(1987); b) W. Oppolzer, Angew. Chem., Int. Ed. Engl., **23**, 876(1984); c) S. Danishefsky and M.P. DeNinno, ibid., **26**, 15(1987); d) D.L. Boger and K.D. Robarge, J. Org. Chem., **53**, 3373(1988) and references therein.

15) For recent attempts to devise exo-selective D-A reaction either by interfering with reaction conditions,a) or modifying substrates,b) see: a) R. Batllori, J. Font, M. Monsalvatje, R.M. Ortuno, and F.S. Ferrando, Tetrahedron, **45**, 1833(1989); b) W.R. Roush, A.P. Essenfeld, J.S. Warmus, and B.B. Brown, Tetrahedron Lett., **30**, 7305(1989).

(Received December 17, 1990)