

Stereoelectronic Control of Cope Rearrangement Energetics through Remote Double Bonds in Novel, Rigid Polycyclic Frames

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The presence and orientation of remote double bonds are shown to completely alter the shapes of Cope rearrangement energy profiles in a heptacyclic system.

In a recent communication, we reported¹ that irradiation (sunlight) of the novel nonacyclic dione **1** gave a photoproduct **2a-c**, through an uncommon photochemical β -cleavage-cyclobutane fragmentation process.² The spectral properties of **2a-c** in solution and the X-ray structure in the solid state were compatible with a Cope-equilibrium process.¹ This interesting finding and the potential synthetic utility³ of the Cope-isomers, prompted us to amplify this observation to closely related systems **3** and **5** and the corresponding saturated polycyclic derivatives **7**, **9** and **11**. We report here a remarkable observation concerning the subtle stereoelectronic effect of the norbornene double bonds and of the disposition of the distal methylene bridges (*syn*- in **1** and **3**, *anti*- in **5**) on the Cope equilibria in these systems.

Irradiation of **1**,³ **3**³ and **5** in ethyl acetate, with sunlight, in a Pyrex vessel for 2–6 h and chromatography (SiO₂) gave **2a-c** (50%), **4a-c** (53%) and **6a** (33%), respectively (Scheme 1). While **2a-c**¹ and **4a-c**[†] exhibited spectral (¹H and ¹³C NMR) properties consonant with the Cope-equilibrium in solution (ambient temp.), **6a**[†] was characterized as a single Cope isomer with bis-enone moieties. The structure of **6a** was further confirmed through an X-ray crystal structure determination (Fig. 1).[‡] The X-ray structure reveals the retention of the cyclobutane ring in **6a**, but with two exceptionally long C–C bonds (≈ 1.64 Å),⁴ reflecting the strain inherent in these systems. Interestingly, **6a** is formed regioselectively during the photochemical reaction and does not equilibrate with the Cope isomers **6b** and **c**.

When saturated nonacyclic diones **7**, **9** and **11** were irradiated under identical conditions, with sunlight, **8b**[†] (80%), **10b**[†] (80%) and **12b**[†] (75%) were obtained and characterized on the basis of the presence of characteristic 6, 6 and 11 lines, respectively, in the ¹³C NMR spectra (Scheme 2). In the saturated series, only the Cope isomers **8b**, **10b** and **12b** with isolated cyclopentene double bonds and without a cyclobutane ring were observed, although their formation necessarily involves initial photocleavage fragmentation of **7**, **9** and **11** to **8a**, **10a** and **12a**, respectively, followed by a Cope rearrangement.

The dramatic differences in the Cope equilibria in these systems may result from differential strain effects and/or electronic participation of the remote double bonds. We have used different computational procedures to probe the relative importance of these factors.

Molecular Mechanics calculations (MM2 force field)⁵ reveal two general patterns in the energetics of the various Cope systems (Table 1). The computed heats of formation indicate a greater exothermicity for rearrangement in **8a**, **10a** and **12a** relative to **2a**, **4a** and **6a**, respectively. The changes in strain energies as well as the results obtained with inclusion of π

Table 1 Calculated reaction energies ($\Delta E/\text{kcal mol}^{-1}$)

Reaction	MM2	AM1	STO-3G//Am1
2a \longrightarrow 2b	–25.7	+14.9	–8.8
8a \longrightarrow 8b	–30.1	+9.7	–15.3
4a \longrightarrow 4b	–20.0	+15.0	–8.7
10a \longrightarrow 10b	–29.9	+9.8	–15.2
6a \longrightarrow 6b	–21.6	+15.8	–6.0
12a \longrightarrow 12b	–27.8	+11.6	–11.8

delocalization effects lead to the same conclusion. While the strain energy differences cannot be attributed to any single dominant steric interaction, the overall trends are consistent with the behaviour expected of medium rings with *trans*-double bonds. The stability (even potential hyperstability) of such systems have been shown to be reduced by transannular interactions involving remote saturated centres.⁶ The observed complete conversion into **8b**, **10b** and **12b** can, therefore, be reconciled with the large strain-energy release following Cope rearrangement. A similar rationale has been provided for the

[†] All compounds were fully characterized on the basis of spectral data and elemental analyses. Selected data for the compounds is given. **3a-c**: δ_{H} (100 MHz, CDCl₃) 6.32 (4 H, br s), 5.49 (4 H, s), 3.12 (4 H, br s), 2.13 (2 H, $\frac{1}{2}$ ABq, J 10 Hz) and 1.80 (2 H, $\frac{1}{2}$ ABq, J 10 Hz); δ_{C} (50.0 MHz, CDCl₃) 208.25, 137.19, 122.00, 46.83 and 41.11. **6a**: δ_{H} (200 MHz, CDCl₃) 6.57 (2 H, dd, $J_1 = J_2$ 1.8 Hz), 6.36 (2 H, br s), 6.10 (2 H, m), 4.14 (2 H, dd, $J_1 = J_2$ 1.8 Hz), 3.48 (2 H, d, J 5.8 Hz), 2.96 (2 H, m), 2.40 (1 H, $\frac{1}{2}$ ABq, J 12.2 Hz), 1.99 (1 H, quint, J_1 5.8, J_2 6.2, J_3 6.0, J_4 6.2 Hz), 1.88 (1 H, $\frac{1}{2}$ ABq, J 8.8 Hz) and 1.65 (1 H, $\frac{1}{2}$ ABq, J 10 Hz). **8b**: δ_{H} (200 MHz, CDCl₃) 5.97 (4 H, s), 2.60–2.43 (4 H, m), 2.39 (4 H, m) and 1.43–1.25 (8 H, series of m); δ_{C} (25.0 MHz, CDCl₃) 207.00, 135.42, 72.41, 39.35, 39.00 and 21.94. **10b**: δ_{H} (100 MHz, CDCl₃) 6.34 (4 H, s), 2.47 (4 H, br s), 1.97 (2 H, $\frac{1}{2}$ ABq, J 10 Hz) and 1.82–1.20 (10 H, m); δ_{C} (50.0 MHz, CDCl₃) 207.65, 132.89 (CH), 74.12, 38.41 (CH₂), 34.94 (CH) and 23.64 (CH₂). **12b**: δ_{H} (100 MHz, CDCl₃) 6.11 (4 H, ABq, J_1 17, J_2 6 Hz), 2.70–2.30 (7 H, series of m), 1.93 (1 H, $\frac{1}{2}$ ABq, J 10 Hz) and 1.66–1.20 (8 H, series of m); δ_{C} (25.0 MHz, CDCl₃) 207.42, 133.65, 132.59, 76.06, 72.24, 39.14, 38.70, 38.47, 34.94, 23.76 and 21.94.

[‡] C₂₀H₁₆O₂ crystallized from dichloromethane–hexane, in the monoclinic system with space group $P2_1/c$, $a = 11.248(1)$, $b = 10.006(2)$, $c = 12.344(1)$ Å, $\beta = 96.979(9)^\circ$, $V = 1379.0(5)$ Å³; $Z = 4$, $D_{\text{cal}} = 1.389$ g cm^{–3}, $\lambda(\text{Cu-K}\alpha) = 1.5418$ Å. Intensity data were collected on an automated Enraf-Nonius CAD-4 diffractometer with graphite monochromated Cu-K α radiation. A total of 2653 reflections were measured, of which 2368 were 'unique'; 1895 of these were 'observed', with $|F_o| \geq 2.0\sigma(|F_o|)$ and were used in the refinement. The structure was solved by SHELX 86¹⁰ and the full matrix least square method with unit weighting scheme. The hydrogen atoms were refined isotropically while the non-hydrogen atoms were refined anisotropically using SHELX 76.¹¹ The refinement converged to a R -factor of 0.056 (5.6%).

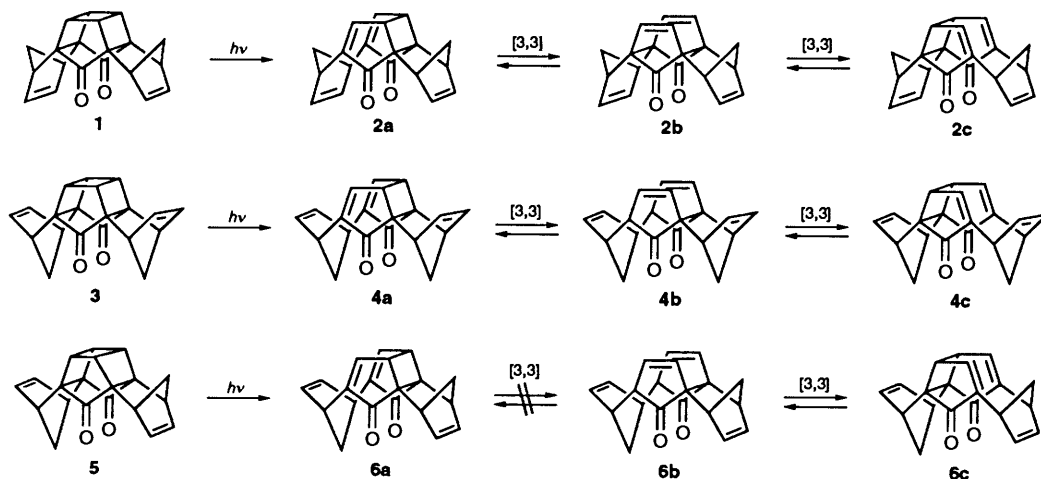
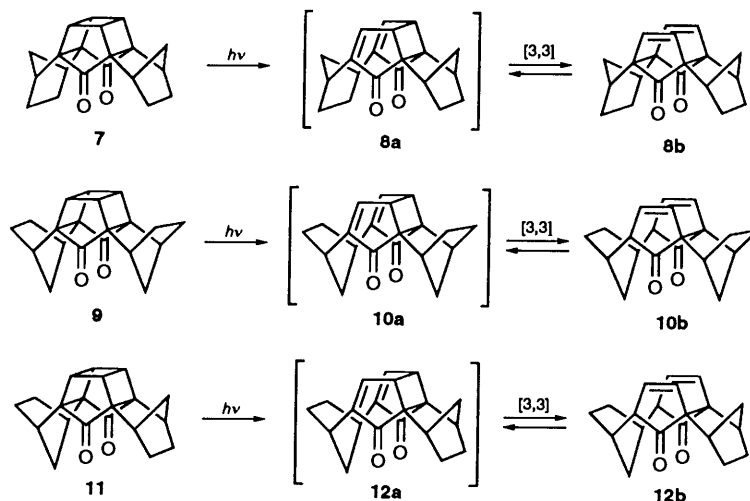
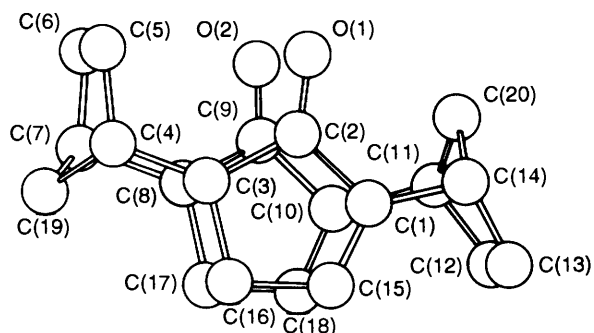
Scheme 1 ($h\nu$, sunlight)Scheme 2 ($h\nu$, sunlight)

Fig. 1 PLUTO diagram of **6a**. Selected interatomic distances (Å): C(1)–C(15) 1.349(5), C(3)–C(8) 1.640(4), C(3)–C(16) 1.533(5), C(8)–C(17) 1.547(5), C(10)–C(18) 1.347(5), C(15)–C(16) 1.483(4), C(16)–C(17) 1.643(5), C(17)–C(18) 1.475(4).

shift in Cope equilibrium in homohydroporphene derivatives on changing the hybridization at the methylene bridge.⁷

While the MM2 energies are consistent with the changes produced by removal of the remote double bonds, the sensitivity of the equilibria to the disposition of the norbornene bridges is not reproduced. The *anti* isomer **6a** is predicted to be not any different from the two *syn* forms **2a** and **4a** as far as the thermodynamic driving force for rearrangement is concerned. Evidently, subtle electronic factors outside the scope of force field methods play a role. We have computed the Cope

rearrangement energy profiles for the six series of compounds using a variety of semiempirical MO methods (MINDO/3, MNDO and AM1).⁸ None of these procedures reproduce the observed variations in the Cope equilibria for the *syn* and *anti* isomers. The failure of these methods may be attributed to the inability of zero differential overlap based methods to account adequately for potential through-space interactions.

The energetics obtained using *ab initio* calculations with the STO-3G basis set⁹ on AM1 optimized geometries are qualitatively consistent with the observed results. The thermodynamic driving force for rearrangement is predicted to be larger on hydrogenating the remote double bonds. More importantly, the *anti* isomer **6a** is computed to have a reduced exothermicity for rearrangement compared to the *syn* forms **2a** and **4a**. Although the energy changes are relatively small, it is possible that the effects noted in the minima will be amplified in the transition state structures. It would then account for the three extreme modes of behaviour of these divinyl–cyclobutane Cope systems. It would be of considerable interest to quantify the electronic effects at the transition states using higher level theory.

In summary, the series of compounds **8a**, **10a** and **12a** are shown to undergo complete Cope rearrangement, while the *anti* isomer **6a** resists the process. The *syn* forms **2a** and **4a** show intermediate behaviour and undergo facile equilibration. The variations result from differing strain energy changes as well as electronic interactions in these substrates.

Experimental

General Procedure.—Irradiation of nonacyclic diones was carried out in N₂-purged ethyl acetate (1 mmol dm⁻³ solution) in a Pyrex vessel by exposure to the mid-day sunlight for 4–6 h. The reaction was monitored by TLC and terminated when an optimum concentration of the product was noticed. Solvent was removed under reduced pressure and the residue was purified through chromatography on a silica gel column. The heptacyclic products were crystallized from dichloromethane–hexane.

Acknowledgements

S. H. K. R. and A. P. thank CSIR for support of their fellowships.

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Paper 3/02938G

Received 24th May 1993

Accepted 24th May 1993