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A CASE OF 2π + 2π CYCLOADDITION OF TWO ENOLATE IONS AT AMBIENT TEMPERATURE

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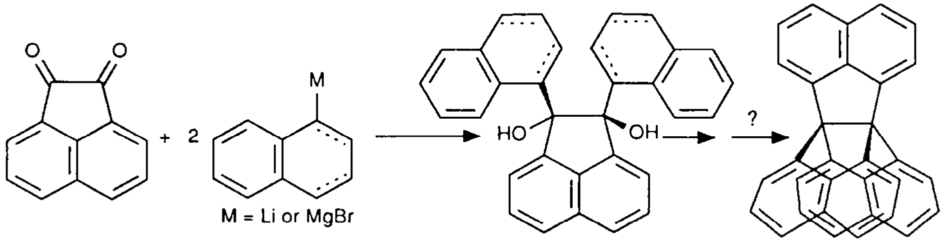
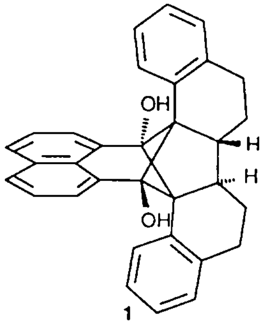
Summary: *Reaction of two equivalents of 1-lithio-3,4-dihydronaphthalene with acenaphthenequinone between 0 °C and 20 °C leads to a derivative of tricyclo[4.3.0.0^{5,9}]nonane by di-oxy-Cope rearrangement followed by the unprecedented "criss-cross" 2π + 2π cycloaddition of the two enolate ions formed.*

During work designed to synthesize trisnaphtho[3.3.3]propellane, we treated acenaphthenequinone with excess (>2 equivalents) of several organolithium and organomagnesium reagents:-



1-Naphthyl magnesium bromide gave the known *trans*-diol[1] but this and the pinacol rearrangement product derived from it failed to cyclise under a variety of the acidic conditions which have been previously used for this type of reaction.[2,3] Even though some extremely rigid systems have been cyclised,[4] we suspected that one cause was poor stereoelectronic alignment for cyclisation, and so we explored the use of less rigid analogues. Amongst these was 1-lithio-3,4-dihydronaphthalene, generated by Shapiro reaction[5] of the 2,4,6-trisisopropylbenzenesulphonylhydrazone[6] of 1-tetralone (1-keto-1,2,3,4-tetrahydronaphthalene). The only product we could isolate in a pure state (in 20% yield) by flash chromatography was clearly not the expected double addition product, *trans*-1,2-bis(3,4-dihydro-1-naphthyl)-1,2-acenaphthenediol, since it contained no vinyl carbon or hydrogen atoms. Instead, signals in the ^{13}C n.m.r. spectrum at 45.9 and 66.8 p.p.m. indicated that these carbons were now sp^3 hybridised. The NMR spectra also indicated two-fold symmetry (either C_2 or C_s) and showed that the protons on the aromatic rings of the tetralyl moieties were sequentially increasingly shielded at 7.04, 6.90, 6.39, and 5.59 p.p.m.[7] This suggested that these rings were placed edgewise over the naphthalene ring.



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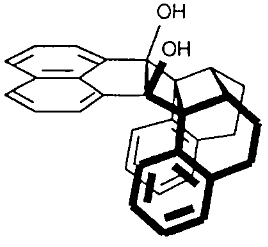

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Two structures,(**1**) and (**2**), which might fit this data are shown above. A firm decision between them and the elimination of other possibilities did not seem practical on spectroscopic grounds alone, although we were inclined towards (**1**) because it was expected that the initial addition step would give a *trans*-adduct and (**1**) could be more reasonably derived from this, and also because it would be less strained.

A single-crystal structure determination has shown that (**1**) is indeed the correct structure for the product. Figure 1 shows the structure, which has approximate (non-crystallographic) C_2 symmetry. In agreement with the NMR evidence, the benzene rings of the tetralyl moieties are in a nearly-perfect edge-face orientation, the closest protons being 2.39±0.05 Å above the naphthalene ring plane. The hydroxyl groups are linked by a network of hydrogen bonds in the crystal.

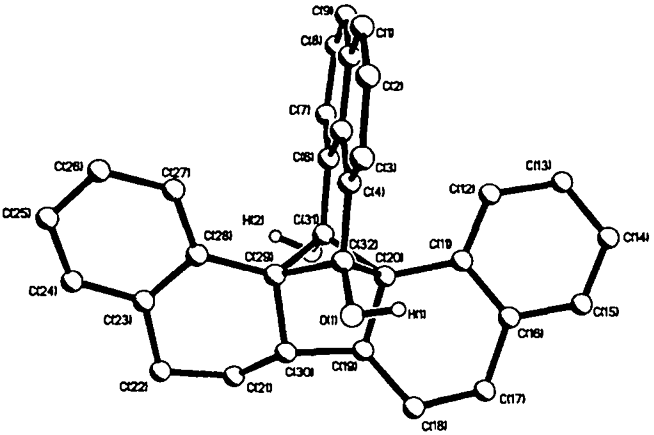

Figure 1 Molecular structure of (**1**) showing atom labelling scheme; hydrogens have not been labelled for clarity.

Although we have not undertaken an exhaustive study of the conditions for and varients of this unexpected reaction, it does seem to be remarkably specific. Thus solutions of 1-phenylvinyllithium and 1-*tert*-butylvinyllithium, generated in each case by a Shapiro reaction exactly as described for the tetralyl derivative, gave no detectable yields of comparable products. In an attempt to probe the minimum temperature for formation of (**1**), the reaction was held at 0 °C until quenching, but while no (**1**) was then formed, alternative products were not successfully isolated.

Experimental

Reaction of 1-Lithio-3,4-dihydronaphthalene with Acenaphthenequinone. A stirred suspension of the 2,4,6-trisisopropylbenzenesulphonylhydrazone[8,9] of 1-keto-1,2,3,4-tetrahydronaphthalene (1-tetralone) (2.12g; 5 mmol) in a 10% solution of tetramethylethylenediamine in hexane (30 ml) was treated dropwise with *sec*-butyllithium (1.2 M in hexanes; 10 mmol) at -70 °C. After stirring for 15 min. the pale yellow solution was allowed to warm up to 0 °C at which temperature nitrogen was evolved and the solution turned dark brown. When gas evolution had ceased (ca. 15min.), acenapthenequinone (0.364 g; 2 mmol) was quickly added and the resulting brown suspension was stirred overnight under nitrogen at ambient temperature. Hydrochloric acid (1 M, 40 ml) was then added and the mixture extracted with ether (3 x 40 ml). The combined organic extracts were washed with water (50 ml), dried ($MgSO_4$), and the solvent then removed under reduced pressure to give a brown oil which was purified immediately by flash chromatography (silica gel: 18 x 5 cm). Ethyl acetate (10%) in light petroleum (b.p. 40-60 °C) eluted the diol (**1**) as a pale yellow solid (0.211 g; 24%). A small sample (ca. 30 mg) was dissolved in ethyl acetate (0.5 ml) and then placed in a diffusion tank containing light petroleum (b.p. 30-40 °C) and left for 3 weeks after which time colourless prisms suitable for X-ray structure determination were obtained, m.p. 223-225 °C. ^{1}H NMR ($CDCl_3$) 7.83 (2H, dd, J 8.2, 1.0Hz), 7.52 (2H, dd, J 7.1, 8.2Hz), 7.43 (2H, dd, J 7.1, 1.0Hz), 7.04 (2H, d, J 7Hz), 6.90 (2H, t, J 7.4Hz), 6.39 (2H, t, J 7.4Hz), 5.59 (2H, d, J 8Hz), 2.97 (4H, m), 2.78 (2H, m), 2.57 (2H, m), 2.26 (2H, m); ^{13}C NMR ($(CD_3)_2CO$) 141.7, 140.5, 134.3, 131.3, 130.1, 129.5, 127.5, 127.1, 127.0, 126.4, 125.1, 122.3, 86.4, 66.8, 43.9, 31.9, 25.7; IR (Nujol) 3501, 3422 cm^{-1} (OH); MS (EI 70 eV) m/e 442(M$^+$, 100%), 424(17), 296(15), 269(39). Anal. Calcd for $C_{32}H_{26}O_2$: C, 86.8; H, 5.9. Found: C, 86.2; H, 6.0.

Crystal Data for (**1**): $C_{32}H_{26}O_2$, $M_r = 442.6$, monoclinic, space group $P2_1/c$ (No. 14), $a = 11.901(3)$, $b = 16.253(5)$, $c = 12.304(5)$ Å, $\beta = 108.59(2)°$, $U = 2255.7(8)$ Å^3, Z = 4, $D_x = 1.303$ gcm^{-3}, $\lambda = 0.71069$ Å, $\mu(\text{Mo-K}_\alpha) = 0.7$ cm^{-1}, F(000) = 936, T = 295 K.

A single crystal of (**1**) (colourless prism, approx. dimensions 0.55x0.45x0.38 mm.) was mounted on a glass fibre in air, and held in place with epoxy glue. All diffraction measurements were made at room temperature (295 K) on a Nicolet R3m diffractometer, using graphite monochromated Mo-K_α *X*-radiation. Unit cell dimensions were determined from 20 centered reflections in the range $14.0<2\theta<27.0°$. A total of 4811 diffracted intensities, including check reflections, were measured in two unique octants (h,k,±l) of reciprocal space for $4.0<2\theta<50.0°$ by Wyckoff ω scans. Three check reflections remeasured after every 50 ordinary data points showed an increase of 4% and variation of ±4% over the period of data collection; an appropriate correction was therefore applied. Of the 4519 intensity data collected, 3992 unique observations remained after averaging of duplicate and equivalent measurements and deletion of systematic absences, of which 3009 having $I>1.5\sigma(I)$ were retained for use in structure solution and refinement. No absorption correction was applied. Lorentz and polarisation corrections were applied.

The structure was solved by direct and Fourier methods and refined with molecules of (**1**) lying in general positions. All non-hydrogen atoms were assigned anisotropic displacement parameters and all hydrogen atoms fixed isotropic displacement parameters. All non-hydrogen atoms and the hydroxy hydrogen atoms H(1) and H(2) were refined without positional constraints. All other hydrogen atoms were constrained to idealised geometries (C-H 0.96 Å, H-C-H 109.5°).

Full matrix least-squares refinement of this model (313 parameters) converged to final residual indices R = 0.048, wR = 0.059, S = 1.69. Weights, w, were set equal to $[\sigma_c^2(F_o)+gF_o^2]^{-1}$, where $\sigma_c^2(F_o)$ is the variance in F_o due to counting statistics and g = 0.0005 was chosen to minimise the variation in S as a function of $|F_o|$. Final difference electron density maps showed no features outside the range +0.19 to -0.15 eÅ^{-3}, the largest of these being close to the hydrogen H(30A) and the midpoints of C-C and C-O bonds. All calculations were carried out on a Nicolet R3m/V structure determination system using programs of the SHELXTL-PLUS package.[10] Complex neutral-atom scattering factors were taken from reference 11. Table 1 lists selected bond lengths and inter-bond angles.‡

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‡ Atomic coordinates, bond lengths and angles, and thermal parameters for (**1**) have been deposited at the Cambridge Crystallographic Data Centre. $R = \Sigma|\Delta| / \Sigma|F_o|$; $wR = [\Sigma w\Delta^2 / \Sigma wF_o^2]^{1/2}$; $S = [\Sigma w\Delta^2 / (N.O.-N.V.)]^{1/2}$; $\Delta = F_o - F_c$

Table 1 Selected Bond Lengths (Å) and Angles (°) for (**1**)

O(1)-C(32)	1.405 (2)	C(9)-C(10)	1.403 (4)	C(20)-C(32)	1.608 (3)
O(2)-C(31)	1.421 (3)	C(11)-C(12)	1.385 (3)	C(21)-C(22)	1.514 (3)
C(1)-C(2)	1.357 (5)	C(11)-C(16)	1.411 (3)	C(21)-C(30)	1.520 (4)
C(1)-C(10)	1.423 (5)	C(11)-C(20)	1.514 (3)	C(22)-C(23)	1.511 (3)
C(2)-C(3)	1.398 (5)	C(12)-C(13)	1.388 (3)	C(23)-C(24)	1.394 (3)
C(3)-C(4)	1.376 (4)	C(13)-C(14)	1.372 (3)	C(23)-C(28)	1.408 (3)
C(4)-C(5)	1.406 (3)	C(14)-C(15)	1.371 (4)	C(24)-C(25)	1.356 (4)
C(4)-C(32)	1.497 (3)	C(15)-C(16)	1.392 (3)	C(25)-C(26)	1.378 (4)
C(5)-C(6)	1.419 (4)	C(16)-C(17)	1.505 (4)	C(26)-C(27)	1.386 (3)
C(5)-C(10)	1.405 (3)	C(17)-C(18)	1.508 (3)	C(27)-C(28)	1.392 (3)
C(6)-C(7)	1.371 (3)	C(18)-C(19)	1.520 (3)	C(28)-C(29)	1.512 (3)
C(6)-C(31)	1.496 (3)	C(19)-C(20)	1.529 (3)	C(29)-C(30)	1.531 (3)
C(7)-C(8)	1.415 (4)	C(19)-C(30)	1.527 (3)	C(29)-C(31)	1.606 (3)
C(8)-C(9)	1.361 (6)	C(20)-C(31)	1.567 (3)	C(29)-C(32)	1.575 (3)

C(5)-C(4)-C(32)	116.2(2)	O(2)-C(31)-C(6)	111.7(2)
C(4)-C(5)-C(6)	117.0(2)	O(2)-C(31)-C(20)	114.2(2)
C(5)-C(6)-C(31)	115.5(2)	O(2)-C(31)-C(29)	116.7(2)
C(20)-C(19)-C(30)	100.8(2)	C(6)-C(31)-C(20)	113.7(2)
C(19)-C(20)-C(31)	101.3(2)	C(6)-C(31)-C(29)	114.8(2)
C(19)-C(20)-C(32)	103.1(1)	C(20)-C(31)-C(29)	83.1(1)
C(31)-C(20)-C(32)	83.6(1)	O(1)-C(32)-C(4)	111.8(2)
C(30)-C(29)-C(31)	104.0(2)	O(1)-C(32)-C(20)	116.7(1)
C(30)-C(29)-C(32)	100.2(1)	O(1)-C(32)-C(29)	115.0(2)
C(31)-C(29)-C(32)	83.4(1)	C(4)-C(32)-C(20)	113.8(1)
C(19)-C(30)-C(29)	100.7(2)	C(4)-C(32)-C(29)	113.9(2)
		C(20)-C(32)-C(29)	82.8(1)

Discussion

The first step in the reaction we have observed must be double addition of 1-lithio-3,4-dihydronaphthalene to produce the dilithio-derivative of the expected *trans*-diol. This is surely followed by a dianionic dioxy-Cope[12] rearrangement to generate a derivative of *trans,trans*-naphtho[1,8:cd]cyclonona-1,6-diene. A close precedent for this stage of the reaction is the first stage of the rearrangement/condensation of 5,6-divinyl-5,6-dihydrochrysene-5,6-diol when treated with KH in refluxing THF to yield 14-oxo-1,2,3.14-tetrahydro-benzo(e)naphth(2,1-g)azulene.[13] In this case, the dioxy-Cope is followed by an aldol reaction, which is not possible in our situation. An overall $2\pi + 2\pi$ cycloaddition of the two enolate ions must then ensue to generate the 1,3-cyclobutanediol dianion. One previous example of a [3,3]-shift followed by $2\pi + 2\pi$ addition to yield the same ring system is know to us. The formation of naphtho[1′,8′]tricyclo[4.3.0.0^{5,9}]nonane (2,1,3-[1]propanyl[3]ylidene-1H-phenalene) was observed[14] during gas phase thermolysis at 400 °C of *cis*-1,2-divinylacenaphthene.

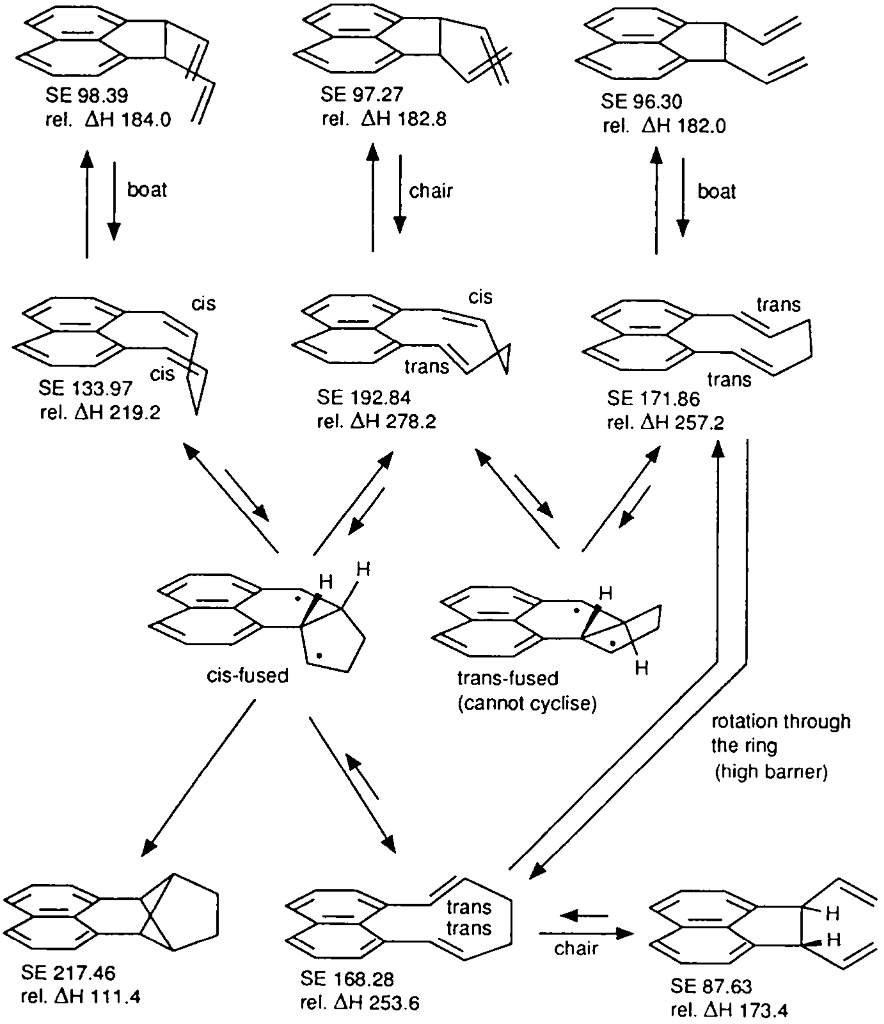
The conditions used by Nelsen and Gillespie were obviously very different from ours, and they also reported that the corresponding *trans*-isomer (the stereochemical equivalent of our species) failed to undergo significant rearrangement. Scheme 1 shows the relationship of these isomers through Cope rearrangements via boat and chair transition states to give various isomers of 9,10-dihydrocyclonona[de]naphthalene, and the subsequent diradical cyclisations.

Wittig and Skipka[15] observed a related rearrangement when they pyrolysed the various isomers of tetrabenzo[*a*,*c*,*g*,*i*]cyclododecene. The *trans,trans*-isomer gave the "criss-cross" product 8b,8c,16b,16c-tetrahydrocyclobuta[1,2-*l*;2,4-*l*′]diphenanthrene in 8% yield. The formation of 1,3:2,4-di(naphth-1′,8′)cyclobutane in 0.1% yield during Wittig reaction of 1,8-bis(triphenylphosphinylmethyl)naphthalene with 1,8-naphthalenedicarboxyaldehyde[16] is more significant in terms of the reaction conditions (boiling diethyl ether). However, it has recently been shown[17].that cyclodeca[1,2,3-*de*:6,7,8-*d′*,*e′*]dinaphthalene claimed to be formed in this reaction and the presumed intermediate in the formation of the cyclobutane is in fact 7,7a-dihydrodibenzo[de,mn]naphthacene.

The formation of (**1**) at such a low temperature raises two interesting but independent questions:-

(a) Is the formation of a cyclobutanediol dianion from two enolate ions thermochemically favourable in general or is this reaction only possible in the present instance because of relief of strain in the presumed intermediate?

(b) Forbidden $2\pi + 2\pi$ additions usually occur via diradical or dipolar intermediates - what is the mechanism here and what factors are responsible for the reaction proceeding under such mild conditions?

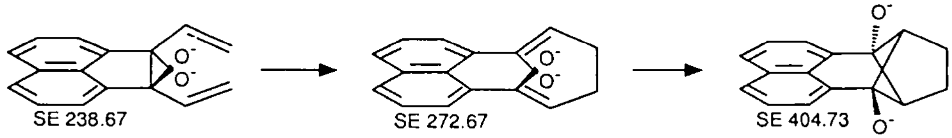


Scheme 1 Steric energies are as calculated by MacroModel, relative values of ΔH are derived as described in the text. All energies are in kJ/mol

The heats of formation and entropies[18,19] of ethene and cyclobutane are such that formation of cyclobutane is mildly favoured at 298 K; ΔG -26.2 kJ/mol, with ΔH -77.9 kJ/mol. Delocalisation in acetaldehyde enol and especially in the enolate ion might well change this situation. Two estimates of ΔH_f for acetaldehyde enol have been reported (-124.7[20] and -127.6 kJ/mol[21]), and an estimate of ΔH_f for cyclobutane-1,3-diol (-307.4) can be reliably made through group equivalent calculations.[22] Thus ΔH for cyclobutane-1,3-diol formation is calculated as between -52 and -58 kJ/mol, so that if the entropy changes remain the same as in the cyclobutane case, ΔG at 298 K would be almost zero. The extra delocalisation in the enolate ion is likely to be quite substantial and may well be worth up to 80 kJ/mol;[23] this would clearly render cyclobutanediol dianion formation unfavourable in the absense of other factors, such as relief of strain. These calculations refer to the gas phase; solvation and the partial ionic character of the metal derivatives might result in a situation in solution somewhere between that for the enol and the enolate ion. The calculations actually suggest the interesting possiblity of reversing the present reaction and generating specific enols by cleavage of cyclobutanediol dianion derivatives. Since cyclobutane-1,3-diones are quite readily available from ketenes, this could have significant utility.

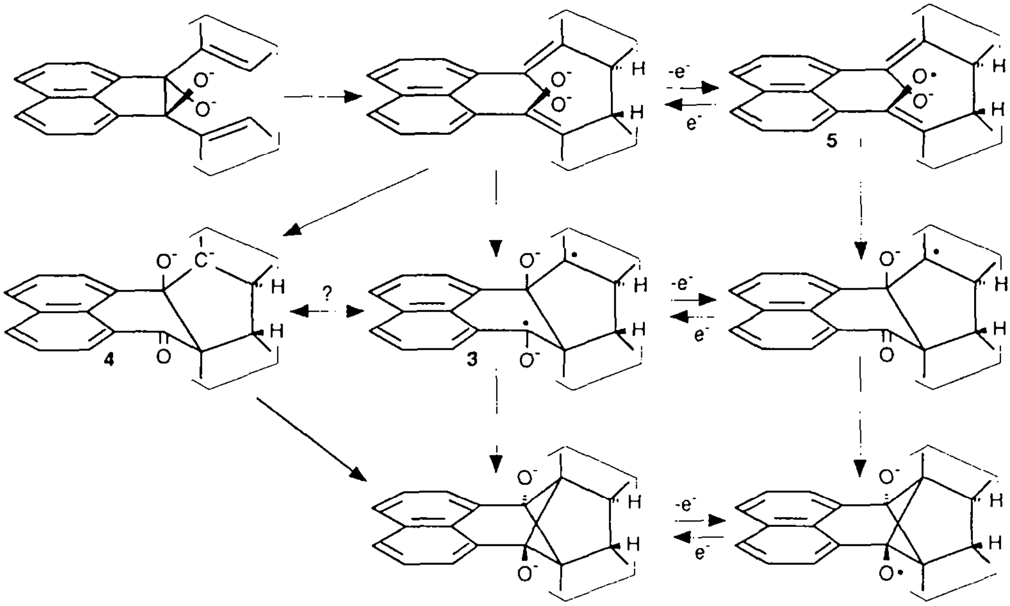
In order to provide some insight into the effects of strain on the energetics of both Nelsen's and our reactions, we have performed molecular mechanics calculations on some of these compounds, using the Macromodel program.[24] The results are included in Scheme 1; because Macromodel does not provide a facility to calculate ΔH_f and also does not use the SCF method as in MMP2[25] for the aromatic system, relative ΔH_f values have been calculated from the steric energies (SE), using the standard MM2[26] heat of formation parameters and ignoring the naphthalene ring carbons. The calculations do show that the Cope rearrangement of the *trans*-isomer through an enforced chair transition state is substantially less favourable thermochemically (by 45 kJ/mol) than that of the *cis*-compound through a boat transition state to the *cis,cis*-product. Examination of models indicates that at least some of the increased strain of the product from the *trans*-isomer will be introduced in the transition state, so Nelsen and Gillespie's[14] observation of lack of rearrangement of this isomer is accounted for, but the surprising ease of our reaction is consequently highlighted. It should be noted that the *trans,trans*-9,10-dihydrocyclonona[de]naphthalene is formed in different conformations from the *cis*- and *trans*-1,2-divinylacenaphthenes, and that these are only interconvertible by rotation of a double bond through the ring, which is likely to be a high energy process.

It is clear that from these calculations that for the hydrocarbons, the overall reaction is highly favourable (by at least 62 kJ/mol), but that the mechanism requires passage through a high-energy strained intermediate. It then becomes clear that in the case of the dianion rearrangement, the delocalisation in the enolate anions of the intermediate will provide stabilisation for this intermediate. It will also presumably lower the energies of the transition states leading to and from that intermediate, thus lowering the barrier to the overall reaction. The results of calculations using Macromodel on the corresponding dianions are shown in Scheme 2; the parameterisation of these species in MacroModel is suspect, but there will be probably cancellation of errors when comparing the initial and final states. According to these calculations, the reaction is still likely to be exothermic overall, and the dienolate intermediate is substantially stabilised, as expected:-



Scheme 2 Rearrangement of dianions according to MacroModel. Steric energies are given in kJ/mol

Turning to the actual mechanism of the cyclobutane ring formation, this forbidden reaction usually proceeds via diradical or dipolar (zwitterionic) intermediates. For our example, these are shown as (3) and (4) in the centre and left-hand column of Scheme 3. We consider that these alternatives are both possibilities under our conditions. It is also conceivable that there is enough through-bond interaction that the true structure of the intermediate is a resonance hybrid of the (singlet) diradical and the anion/ketone. Alternatively, the reaction could involve intramolecular electron transfers. It is now well-established that cycloadditions of radical ions are often extremely fast.[27] In this case, oxidation of the dienolate by unreacted acenapthenequinone would give the radical anion (5) shown on the right-hand side of Scheme 3 which could perhaps complete the bond formation steps via low barriers before reverse electron transfer yielded the final dianion. We do not think our data allow us to make a firm decision between these possibilities.



Scheme 3 Possible mechanisms for the 2π + 2π cycloaddition of two enolate ions. The tetralyl groups have been omitted for clarity.

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