

## Cyclopentadienone Oxime Dimers as Precursors to Cyclone Equivalents

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Monomerisation (110–150 °C) of the stereoisomeric mixture of the dioxime **6a**, or its ethers or esters, **6b–e**, gives the oximes **7** which can be trapped by a wide range of dienophiles to give good yields of the adducts **8–12**; deoximation of these to the ketones can be effected by catalytic hydrogen transfer (Pd/C, cyclohexadiene) as a mild alternative to acid hydrolysis.

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Cyclopenta-2,4-dienones (cyclones) lacking  $\alpha$ -substituents are extremely reactive towards dimerisation, which occurs irreversibly, and much less so towards cycloaddition to other substrates.<sup>1</sup> Attempts to intercept the parent cyclone **1** in Diels–Alder reactions have been largely unsuccessful, and exceptions have required the use of large amounts of trapping agent.<sup>2–4</sup>

Masked versions of **1** are its methyl or ethyl ketal, which have proved to be valuable synthetic intermediates,<sup>5</sup> and the

fulvenes **2**.<sup>6</sup> Adducts from these can be converted into the bridged ketone, but the conditions required (*e.g.* acids and ozonolysis, respectively) are often severe or are not conducive to the preservation of the residual Diels–Alder double bond.

The instability of **1** is commonly attributed to its anti-aromaticity (*cf.* **1b**). As *Z* becomes more tolerant of positive charge the contribution from **c** should lead to increased stabilisation. Thus, fulvenes **2** are stable but very reactive, and

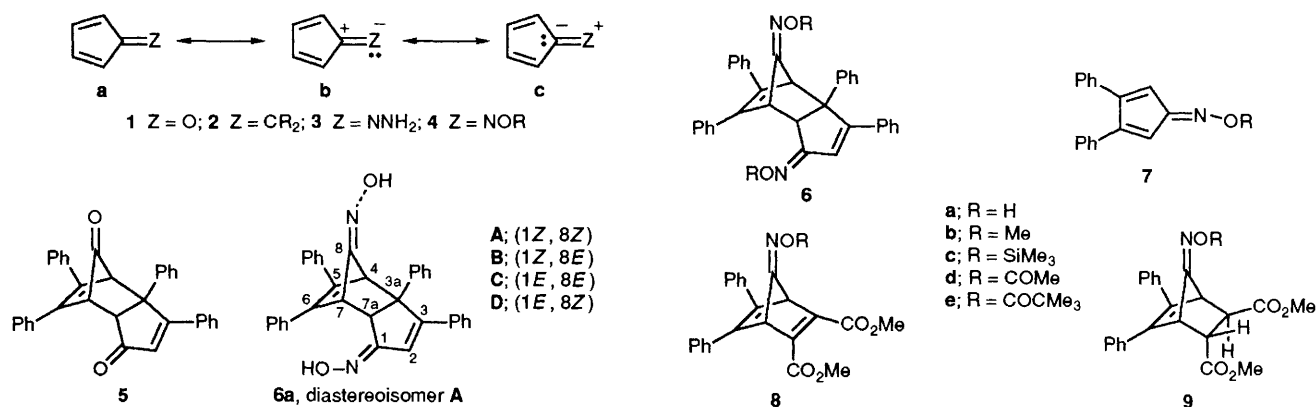


Table 1 Adducts 8–12 of oximes 7

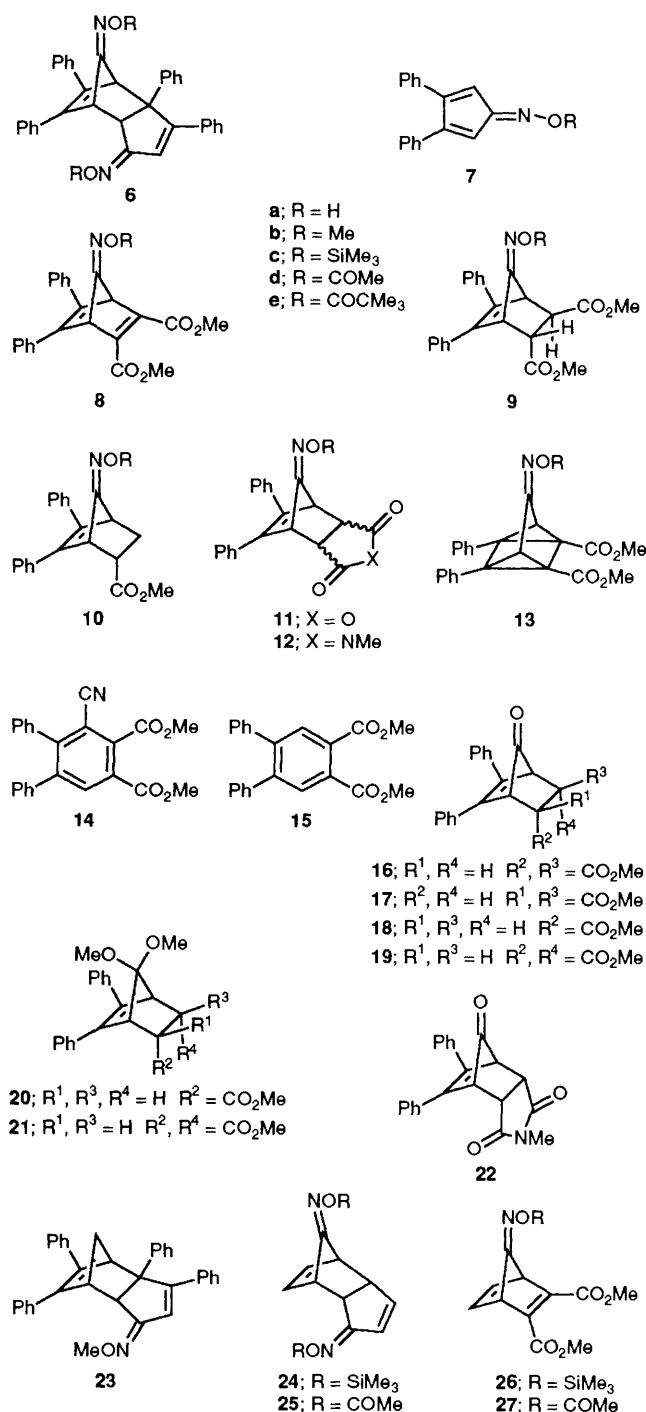
Adduct	Yield (%) <sup>a</sup>	Diastereoisomeric ratio <sup>c,d</sup>
8b	76	
8c	>90 <sup>b</sup>	
8d	66	
8e	48	
9a	44	1:1, <i>E</i> : <i>Z</i>
9b	51	1:1, <i>E</i> : <i>Z</i>
9c	>90 <sup>b</sup>	1:1, <i>E</i> : <i>Z</i>
9d	37	1:1, <i>E</i> : <i>Z</i>
10b	91	1:1, <i>E</i> : <i>Z</i>
10c	70 <sup>b</sup>	1:1, <i>E</i> : <i>Z</i>
10d	70	1:1, <i>E</i> : <i>Z</i>
11b	52	1:1.3, <i>endo</i> : <i>exo</i>
11d	61	2:1, <i>endo</i> : <i>exo</i>
12c	>90 <sup>b</sup>	5:1, <i>endo</i> : <i>exo</i>

<sup>a</sup> After chromatography, unless otherwise stated. <sup>b</sup> Isolated directly, 8c as an oil, 9c, 10c and 12c as crystalline diastereoisomeric mixtures. <sup>c</sup> Approximate ratios, determined by <sup>1</sup>H NMR spectroscopy. Compounds 8 are racemic, 9–12 are diastereoisomeric mixtures; 9 and 10 are designated as *E/Z*, rather than *anti/syn*, and thus, stereochemistry is unambiguous. <sup>d</sup> The following stereoisomers were obtained pure as crystalline solids: *Z*-9b, decomp. >170 °C; *Z*-9d, m.p. 162–164 °C; *endo*-11b, m.p. 149–152 °C; *exo*-11b, m.p. 162–163 °C; *endo*-11d, decomp. >185 °C; *endo*-12c, m.p. 127.5–128.5 °C.

the hydrazones 3 are described as stable but quite inert.<sup>7</sup> Intuitively it seems reasonable that the oximes 4 would be intermediate in stability between the cyclone and its hydrazones, and this is supported by theoretical considerations.<sup>8</sup> Predictably their stability might be such that, in contrast to 1, they could be prepared by thermolysis of their dimers. In the event that they would have to be reacted *in situ*, *i.e.* were too unstable for isolation, this would avoid the need to make them from a monomeric precursor under likely very harsh conditions (*e.g.* elimination by strong acid or base from hydroxy- or halogeno-cyclopentenone oximes), which might be unsuitable for the maintenance of the monomer itself or its cycloaddition partners. Using the oximes of the dimer of 3,4-diphenylcyclopentadienone as a test case we show here that this indeed provides a feasible route to cyclone equivalents.

Treatment of the *endo* dimer 5, the sole product of irreversible dimerisation of the diphenylcyclone, with an excess of hydroxylamine (pyridine–MeOH, reflux)<sup>9</sup> gave a mixture of the four possible diastereoisomers of 6a of which two, the (1*Z*, 8*Z*), A, and (1*Z*, 8*E*), B, dominated (>90%, 3:1). These could be purified with difficulty by fractional crystallisation.† They were assigned their structures on the

† The original reference<sup>9</sup> describes two isomers, m.p. 176 and 229 °C. We obtained pure samples of each of 6a, A, B and D, but all decomposed before melting.



basis of an X-ray crystallographic determination of the dipivalate of B (Fig. 1),‡ together with comparative high resolution proton NMR spectral analysis of each of A, B and C, and of the total mixture.

‡ Crystal data for the dipivalate (1*Z*, 8*E*)6c: C<sub>44</sub>H<sub>42</sub>N<sub>2</sub>O<sub>4</sub>, *M* = 662.8, monoclinic, space group *P*2<sub>1</sub>/*c*, *a* = 20.437(6), *b* = 11.346(4), *c* = 17.665(5) Å, β = 114.90(2)° *U* = 3715(2) Å<sup>3</sup>, *Z* = 4, *D*<sub>c</sub> = 1.185 g cm<sup>-3</sup>, *F*(000) = 1408, λ = 0.71073 Å, *T* = 200 K, μ(Mo–Kα) = 0.70 cm<sup>-1</sup>. Data were collected from a colourless prism of dimensions 0.44 (100,  $\bar{1}$ 00) × 0.48 (11 $\bar{1}$ ,  $\bar{1}$ 1) × 0.40 ( $\bar{1}$ 11, 111) mm on a Siemens R3m/V diffractometer by the ω scan method (4.0 < 2θ ≤ 50°). The structure was solved by direct methods using 4087 observed data [*F* ≥ 6σ(*F*)] from 6542 independent reflections and refined by full-matrix least-squares to *R* = 0.0417 and *R*<sub>w</sub> = 0.0630. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

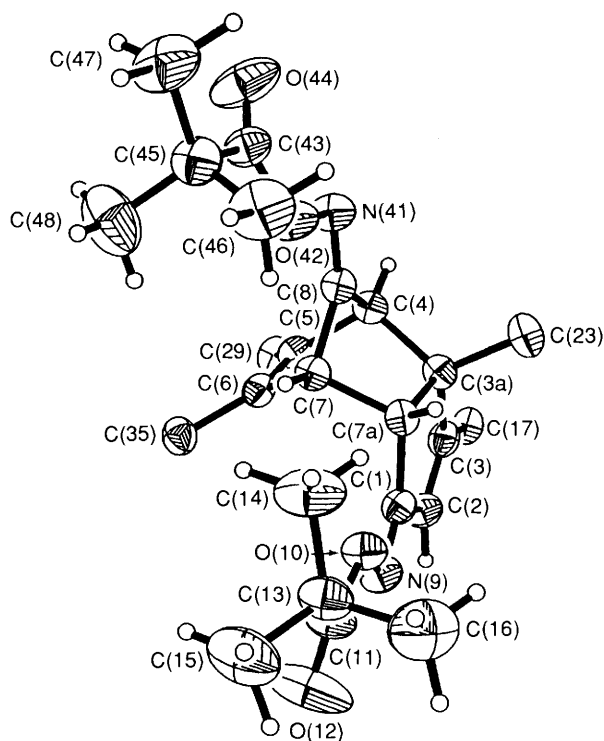


Fig. 1 Molecular structure of the dipivalate (1*Z*,8*E*)-**6e**, showing only the *ipso* carbon atoms of the phenyl groups, C(17), C(23), C(29) and C(35)

Methoxyamine gave a similar mixture of the methyl ethers **6b**. The oxime **6a** could be directly silylated to **6c** ( $\text{Me}_3\text{SiCl}$ ) and acylated to **6d** and **e** ( $\text{Ac}_2\text{O}$ ,  $\text{Me}_3\text{CCOCl}$ ), the products in every case reflecting the stereoisomeric composition of the starting oxime.

The stereoisomerism in **6a–e** is of no consequence in their thermal reactions. Refluxing in toluene (up to 18 h) or in bromobenzene (up to 2 h) gave the transient monomer **7** in each case which reacted smoothly with a variety of substrates: dimethyl acetylenedicarboxylate, dimethyl fumarate, methyl acrylate, maleic anhydride and *N*-methylmaleimide. Rate studies showed that in the reaction with an excess of dimethyl acetylenedicarboxylate there are no large substituent effects in **6**, although ethers generally react faster than esters. §

The structures and yields of the Diels–Alder adducts **8–12** are shown in Table 1. The free oxime **6a** reacted cleanly only with dimethyl fumarate, other dienophiles giving complex products, but adducts of **6a** could in general be made by desilylation of the trimethylsilyl ethers on silica gel.

In the adducts from **7** the oxime group generates in principle two stereoisomers (*synlanti*) from dimethyl fumarate, two (*endolexo*) from the cyclic dienophiles, and four (*synlanti*, *endolexo*) from methyl acrylate. With the fumarate there was no stereoselectivity (*syn*:*anti*, 1:1), with the anhydride very little (*endo*:*exo*, 1:1.3 for ethers, 2:1 for esters), and with the maleimide a strong *endo* bias (5:1 in **12c**, only adduct made). Methyl acrylate gave complete *endo*, but no *syn–anti* selectivity.

The proof of structure of the adducts followed from their NMR spectra, especially the W coupling of the bridgehead protons, and, where relevant, the large difference in coupling constant between a bridgehead proton and its vicinal *endo* vs. *exo* neighbour. In adducts from dienophilic methyl esters an

*endo* OMe group was strongly shielded by the closer phenyl group (e.g.  $\delta$  OMe 3.76, 3.20 in **9d**).

All of the norbornadienone oximes **8** could be cyclised by sunlight to the quadricyclanone oximes **13**, and the esters, e.g. **8d**, could be aromatised to the cyanophthalate **14** by heating with acid.

The objective of trapping the cyclone is completed by deoxygenation of the adducts. As expected acidic conditions were successful, HCl (1 mol  $\text{dm}^{-3}$ ) in MeOH converting **8b** and **d** and **13b** into the phthalate **15**. Ketone formation was straightforward in the case of **9** (**a**, **b** and **d**) and the *exo* anhydride **11b**, which gave the diesters **16** and **17**, respectively, but was plagued by competitive ketalisation in the case of the less hindered oximes **10b** and *endo* **11b** which gave **20** and **21**. Deketalisation of these to **18** and **19** could, however, be achieved with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ .

We also found that the ketone could be generated in most cases under neutral conditions by catalytic hydrogen transfer on Pd-charcoal with cyclohexa-1,3- or 1,4-diene in refluxing MeOH, thus allowing the potential synthesis of cyclone adducts containing acid sensitive groups. Ethers or esters could be used. Excellent yields of **16** were obtained from any of **9a–c**, *synlanti* **9c** going to **16** by way of *synlanti* **9a**. *Synlanti* **10c** gave the keto ester **18**, and the *endo* silyl ether **12c** gave the keto imide **22**. ¶ The ketimine is assumed to be an intermediate in all these reactions.

With cyclopentadiene the cyclone oxime ethers act as  $2\pi$  components, paralleling the behaviour of the oxime itself.<sup>4</sup> Thus **6b** gives *synlanti* **23** (1:1) of assumed *endo* stereochemistry. Oxime esters are unreactive.

Preliminary experiments with the parent, ring unsubstituted, oxime dimers show that the approach described here is quite general and that the oximes **4** are readily available. The stereoisomeric mixtures of ethers **24** and esters **25**, obtained from the cyclopentadienone oxime dimer,<sup>10</sup> also monomerise on heating. With dimethyl acetylenedicarboxylate at 130 °C the rate of formation of **26** from **24** is comparable to that of **8c** from **6c**, but that of **27** from **25** is at least an order of magnitude slower than that of **8d** from **6d**. Electronic and/or steric factors are clearly much more important in the ring unsubstituted oxime dimers than in the case of dimers **6**. Whether this is so in the thermolysis to **4**, or in the reaction of **4** itself, has yet to be determined.

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§ Rate studies on individual stereoisomers are complicated by the fact that above 80 °C isomers **A** and **C** are rapidly Cope interconvertible while each of **B** and **D** is Cope degenerate.

¶ The following ketones and ketals were obtained pure as crystalline solids: **16**, m.p. 114–115 °C; **17**, m.p. 178–180 °C; **18**, m.p. 139–140.5 °C; **21**, m.p. 144–145 °C; **22**, m.p. 180–181 °C.