Stereochemistry of a Cyclopropanone by Crystal Structure Analysis. The *Exo* Configuration of the Diels–Alder Adduct of Cyclopropenone and 1,3-Diphenylisobenzofuran Appears To Be Stabilized Relative to the *Endo* by an Attractive Ether–Carbonyl Interaction

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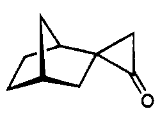
We recently reported[1] that the diastereomeric cyclopropanones **1** and **2** undergo facile interconversion at subambient temperatures. The kinetics of this process provide an approximate measure of a cyclopropanone–oxyallyl energy separation ($\sim$19 kcal/mol). In the course of searching for other synthetically accessible pairs of stereoisomeric cyclopropanones, we noted that the [4 + 2] cycloaddition of cyclopropenone with 1,3-diphenylisobenzofuran (DPIBF), discovered by Breslow and co-workers,[2,3] potentially could yield both *exo* (**3**) and *endo* (**4**) adducts. These stereoisomers would be expected to interconvert in the same fashion as **1** and **2**, through rupture of the C–C bond opposite the cyclopropanone carbonyl carbon. For this reason, we were intrigued by the report[2,3] that the product of the cyclopropenone–DPIBF reaction showed a single nonaromatic proton NMR signal at 2.75 ppm ($CDCl_3$), apparently indicating the presence of only one isomer.



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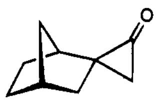

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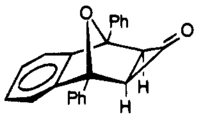

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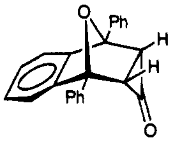

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The carrier of the NMR signal was drawn by Breslow and co-workers as the *exo* structure **3**.[3] The present communication describes a single-crystal X-ray structural analysis which supports this assignment and suggests a rationale for the exclusive observation of **3**. We also briefly describe our efforts to locate the elusive *endo* isomer **4** and measure the rate of its interconversion with **3**.

Since **3** and **4** were expected to interconvert rapidly at room temperature, we proposed that the single NMR resonance observed[4] probably reflected an unsymmetric equilibrium between the two stereoisomers rather than a kinetic preference for the Diels–Alder reaction. Following this assumption, we were led to wonder what the source might be of the putative thermodynamic preference for **3** over **4**. Inspection of AM1-RHF[5] geometries suggested that the *exo* isomer **3** contained an intramolecular interaction between the bridging oxygen and the carbonyl carbon of the cyclopropanone, whereas the *endo* isomer **4** did not.

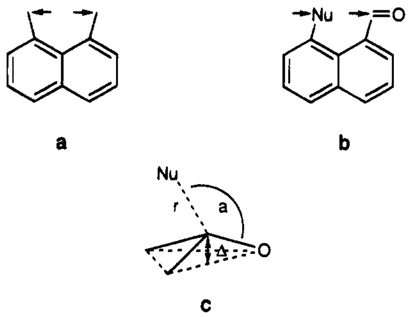

Figure 1. Distortions in 1,8-disubstituted naphthalenes. (a) Repulsive steric interaction leading to "splayed-out" substituents. (b) Attractive nucleophile–carbonyl interaction. (c) Parameters describing the nucleophile–carbonyl interaction.

This type of interaction has been extensively studied in crystal structures, most notably by Bürgi, Dunitz, and co-workers.[6-11] For example, they showed[11] that while typical 1,8-disubstituted naphthalenes adopt a "splayed-out" geometry due to steric repulsions (Figure 1a), in cases where one substituent possesses a nitrogen or oxygen lone-pair and the other a carbonyl function, a distorted geometry such as that in Figure 1b results.

Taken as a whole, these observations reflect (within certain geometric constraints/preferences) a *stabilizing, attractive* interaction[11] between the nucleophilic and electrophilic centers in Figure 1b. With reference to Figure 1c, the distinguishing characteristics are seen to be a nonbonded distance *r* approaching van der Waals contact ($\sim$2.6 Å), a slightly obtuse angle *a* of approach (94–107°), and some pyramidalization at the carbonyl carbon ($\Delta = 0.02$–0.04 Å). If **3** contains this set of features (suggested to be a static model for an incipient nucleophilic addition), it seems reasonable that it should be favored energetically relative to **4**.

X-ray analysis of a crystal of the cyclopropenone–DPIBF adduct now confirms its structure as **3** and clearly demonstrates the nucleophile–carbonyl interaction. Passage of a supersaturated solution of **3** (made according to a variant of the original procedures of Breslow and co-workers[2,12]) in diethyl ether ($\sim$0.1 M) through a Pasteur pipet containing a plug of glass wool leads to the formation of diffraction quality crystals. The resulting structure of **3**, the first for a cyclopropanone, is shown in Figure 2.

The relationship between the bridging oxygen O2 and the cyclopropanone carbonyl defined by C1 and O1 is appropriate for the ether–carbonyl interaction proposed above. Referring to Figure 1c, $r = 2.54$ Å, $a = 121°$, and $\Delta = 0.035$ Å (distance of C1 from the plane defined by O1, C11, and C2). Although *a* is at least 10–15° more obtuse than normal, examples of deviations this large are known.[7]

Bürgi *et al.* have noted that the net energetic effect of close approach of an oxygen or nitrogen lone-pair to carbonyl should

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[1] Cordes, M. H. J.; Berson, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 11010.

[2] Breslow, R.; Oda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4787.

[3] Oda, M.; Breslow, R.; Pecoraro, J. *Tetrahedron Lett.* **1972**, 4419.

[4] If the barrier to ring-opening were low enough (<10 kcal/mol), the signal could be due to a weighted average of the resonances of **3** and **4**. In that case, changes in NMR line shape upon cooling would have been expected, but we did not find such effects in spectra observed at temperatures down to −78 °C in several solvents.

[5] Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

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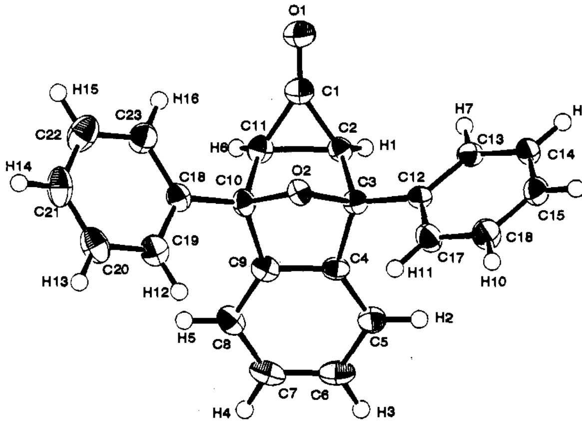


Figure 2. Crystal structure of 3.

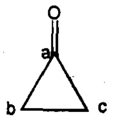
reflect some balance between beneficial factors (e.g., electrostatics, overlap) and the costly factor of pyramidalization.[7] We suggest, however, that pyramidalization of a cyclopropanone carbonyl, as in **3**, is likely to be less costly than usual, because it relieves the strain of a planar trigonal center in a three-membered ring.

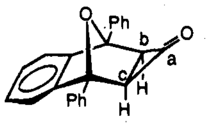
The stability of **3** relative to **4** is thus conveniently rationalized as a consequence of a transannular attraction. Among other factors likely to contribute to this preference are torsional effects around the bond joining the three-membered ring to the remainder of the polycyclic structure. The *endo* isomer is closer to having an eclipsed conformation.[13]

Apart from the crystal structure of **3**, a microwave spectrum of the parent compound obtained by Pochan *et al.*[14] is the only source of detailed structural information for the strained cyclopropanone moiety. Table 1 contains a comparison of the two experiments. The geometries are quite similar.

Finally, we have made several attempts to observe the *endo* isomer **4**. In support of the status of **3** as the product of thermodynamic control, heating **3** in toluene-d_8 to 70−80 °C in an NMR probe does not lead to observation of a second nonaromatic resonance. However, mixing ~5 mg of cyclopropenone and ~25 mg of DPIBF in ~0.5 mL of CD_2Cl_2 at −30 °C (conditions under which the cycloaddition takes several hours to complete) leads to the observation of a small singlet at 3.30 ppm of 1−2% the intensity of the principle peak (due to **3**) at 2.86 ppm. The small peak grows in as the starting materials are consumed, but as the reaction approaches completion, its relative intensity begins to diminish. Upon warming the solution above −20 °C, the small peak disappears quickly.

Table 1. Comparison of Microwave and Crystal Structure Data on Cyclopropanones





3

geometric parameter	parent by microwave	**3** by crystal structure
O−C$_a$ distance	1.19	1.200
C$_a$−C$_b$ distance	1.475	1.469
C$_b$−C$_c$ distance	1.575	1.592
C$_b$−C$_a$−C$_c$ angle	65	65.5

We believe that the small peak is in fact due to the missing *endo* isomer **4**, which then converts to **3** through a ring-opening reaction with a half-life of about 1 h at −30 °C. This rate is of the same order of magnitude as that observed for the conversion of **1** to **2** in diethyl ether.[1] The Diels−Alder reaction therefore has a kinetic preference for formation of **3** over **4** of perhaps 50:1, a composition which slowly changes to an even larger thermodynamic preference for **3**.

Although the evidence for the assignment of the small transient peak to **4** is circumstantial, we consider it persuasive. The chemic shift relative to **3** (about 0.5 ppm downfield) is consistent with expectations based on related systems.[12] Further, we are hard pressed to devise an explanation other than that given above for the appearance of the minor component's resonance simultaneously with that of **3** and its subsequent disappearance upon standing or warming.

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Supplementary Material Available: Detailed X-ray diffraction data for compound **3** (15 pages); observed and calculated structure factors (10 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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