Why Is the Diels–Alder Adduct between Difluorocyclopropenone and 1,3-Diphenylisobenzofuran So Reactive? An ab Initio Molecular Orbital Study of the Ring Opening of *cis*-2,3-Difluorocyclopropanone

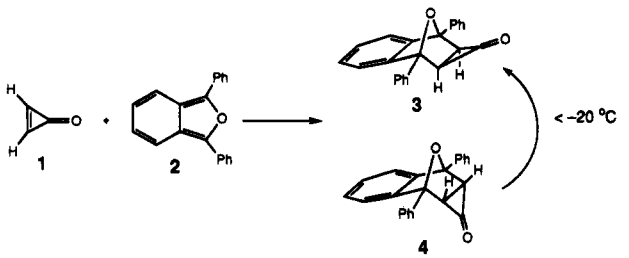
Carolyn A. Jacobs and William P. Dailey*

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104-6323

Received June 27, 1995[⊗]

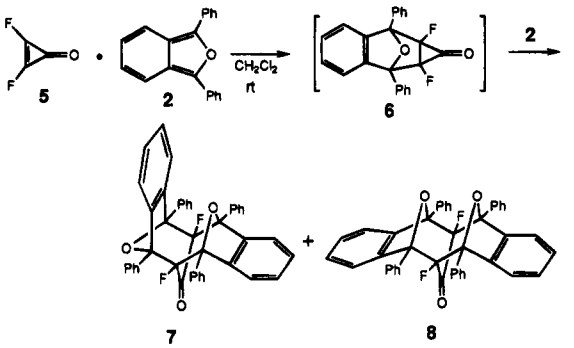
Reaction of difluorocyclopropenone (**5**) and diphenylisobenzofuran (**2**) yields the two isomeric 1:2 cycloadducts **7** and **8** in a ratio of 9:1. The structure of the major isomer was determined by X-ray crystallography and was shown to be the unsymmetrical one. The minor isomer is assigned a symmetrical structure based on spectroscopic data. Attempts to observe the initial 1:1 Diels–Alder adduct **6** were unsuccessful because of the low reactivity of difluorocyclopropenone and the high reactivity of the presumed intermediate difluorocyclopropanone **6**. As an aid in the investigation, ab initio calculations were carried out on the ring-opening reaction of the parent *cis*-2,3-difluorocyclopropanone (**11**) to the corresponding oxyallyl species **13**. The results are compared with previous theoretical and experimental work. *cis*-2,3-difluorocyclopropanone is calculated to have a much smaller barrier (12–14 kcal/mol) to ring opening than the parent cyclopropanone (22–28 kcal/mol).

The recent experimental[1] and computational[2] reports on the cyclopropanone system together with the report of the X-ray structure of a cyclopropanone[3] have prompted us to report our results related to the *cis*-2,3-difluorocyclopropanone system. Our synthesis and isolation of difluorocyclopropenone[4] has allowed us to investigate several reactions of this compound. The parent cyclopropenone (**1**) undergoes Diels–Alder reaction with 1,3-diphenylisobenzofuran (**2**) to produce a 1:1 cycloadduct in quantitative yield.[5] This 1:1 cycloadduct was found



to be stable at 100 °C for extended periods of time. Recently, Berson and co-workers[3] have reported the X-ray crystal structure for this cycloadduct and demonstrated that it had the exo configuration (**3**). They also presented spectroscopic evidence for the endo adduct (**4**) which isomerized below room temperature to the more stable exo one. We therefore examined the analogous reaction of difluorocyclopropenone with **2** in the hope of obtaining evidence for the corresponding difluorocyclopropanone.

Stirring a methylene chloride solution of equal molar quantities of difluorocyclopropenone (**5**) and 1,3-diphenylisobenzofuran (**2**) at room temperature overnight resulted in the formation of two new products in a 9:1 ratio as determined by ^{19}F NMR. The two products were easily separated using a combination of trituration and flash column chromatography. X-ray crystallographic analysis[6] of the major product demonstrated that it was the unsymmetrical 1:2 adduct **7** between **5** and **2**.



On the basis of spectroscopic evidence, the structure of the minor product was determined to be the symmetrical 1:2 adduct **8**. Mass spectrometry indicated that it, like **7**, was a 1:2 adduct between **5** and **2**. Furthermore, ^{13}C NMR and ^{1}H NMR data were consistent with a symmetrical compound. Compelling evidence for the symmetrical structure was based on the number of carbon atoms coupled with fluorine. Both the carbons directly bonded to fluorine, and those adjacent to the CF group were coupled. Compound **7** exhibits three carbon-fluorine doublets and one triplet whereas the minor product, **8**, displays only two such doublets as well as one triplet. The symmetrical isomer **8** was chosen over the other possible symmetrical 2:1 adduct **9** based on the severe steric interactions between the two benzo groups predicted by molecular models for **9**.

[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1995.

(1) (1) (a) Sorensen, T. S.; Sun, F. *J. Am. Chem. Soc.* **1995**, *117*, 5592. (b) Cordes, M. H.; Berson, J. *J. Am. Chem. Soc.* **1992**, *114*, 11010.

(2) (a) Lim, D.; Hrovat, D. A.; Borden, W. T.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1994**, *116*, 3494. (b) Coolidge, M. B.; Yamashita, K.; Morokuma, K.; Borden, W. T. *J. Am. Chem. Soc.* **1990**, *116*, 3494.

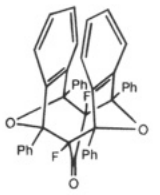
(3) Cordes, M. H. J.; de Gala, S. Berson, J. *J. Am. Chem. Soc.* **1994**, *116*, 11161.

(4) Jacobs, C. A.; Brahms, J. C.; Dailey, W. P.; Beran, K.; Harmony, M. D. *J. Am. Chem. Soc.* **1992**, *114*, 115.

(5) (a) Breslow, R.; Oda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4787. (b) Oda, M.; Breslow, R.; Pecoraro, J. *Tetrahedron Lett.* **1972**, 4419.

(6) The results of the X-ray structure determination have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

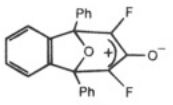
0022-3263/95/1960-7747$09.00/0



9

In an effort to determine whether the 1:1 adduct **6** could be observed in the above reaction, low-temperature ^{19}F NMR experiments were conducted using a several-fold excess of **5**. At −30 °C, the reaction between **2** and **5** did not proceed. At 0 °C the reaction did proceed very slowly, but the buildup of an intermediate was not observed. Only **7** and **8**, the 1:2 adducts, were observed.

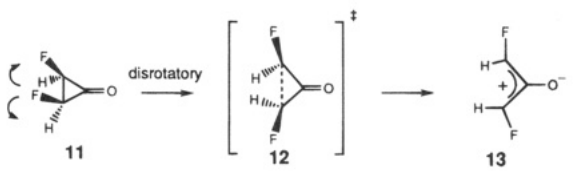
The formation of **7** and **8** can be rationalized by proposing that the initial (unobserved) Diels−Alder adduct **6** undergoes ring opening to oxyallyl **10** faster than it is formed and that **10** reacts quickly with more **2**. The



10

reaction of cyclopropanones in cycloaddition reactions is well known and most likely occurs via the corresponding oxyallyl.[7] While isomerization of *trans*-2,3-di-(*tert*-butyl)-cyclopropanone has been measured to be 28−30 kcal/mol,[8] values for the isomerization of *cis*-2,3-di-(*tert*-butyl)cyclopropanone[1a] and a spiro-substituted cyclopropanone[1b] are much lower (13 and 19 kcal/mol, respectively). These three processes are believed to occur via the corresponding oxyallyl. Recently, ab initio calculations have been reported for the ring opening of cyclopropanone and 2,2-dimethylcyclopropanone to the corresponding oxyallyl.[2] 2,2-Dimethylcyclopropanone was predicted to have a barrier to ring opening about 2 kcal/mol lower than the parent.[2a] An early semiempirical study[9] on the ring opening of substituted cyclopropanones concluded that substituted cyclopropanones open more readily than the parent compound, and that fluorine enhances ring opening more than alkyl substitution.

Ab Initio Calculations. As an aid to understanding the high reactivity of the (presumed) initially formed *cis*-difluorocyclopropanone **6**, ab initio calculations[10] were carried out on the model system *cis*-2,3-difluorocyclopropanone (**11**), the transition structure for its disrotatory ring opening (**12**), and the corresponding oxyallyl species (**13**). Of the two different possible disrotatory pathways,



11 12 13

only the one in which the fluorine atoms were rotated out was followed since this is the only disrotatory mode that would be geometrically possible in reaction of **6**. The computational method used was very similar to that

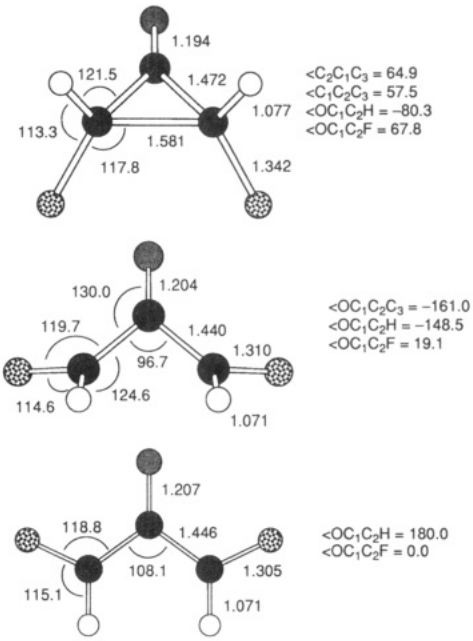


Figure 1. Calculated geometries for *cis*-2,3-difluorocyclopropanone (**11**, top), the transition structure for disrotatory ring opening (**12**, middle), and the corresponding oxyallyl (**13**, bottom) using CAS(4/4)/6-31G** calculations. Distances in angstroms and angles in degrees.

reported by Borden and co-workers[2] and involved a CAS-(4/4) wavefunction using the 6-31G** basis set. The active space for singlet $^1A_1$ oxyallyl consisted of distributing the four π electrons between the four pi molecular orbitals. This active space leads naturally to an active space for cyclopropanone that involves the π and π^* orbitals of the C=O and the σ and σ^* orbitals for the C2−C3 bond that is broken in the transition state. The structures were fully optimized and are shown in Figure 1. Numerical frequency calculations confirmed the nature of the stationary points and produced values for zero point vibrational energy. Single point energy calculations were carried out on the structures using CASPT2N calculations.[11] The CASPT2N calculation is a method of evaluating the MP2-level electron correlation correction to the CASSCF energy. The total energies, ZPE, and relative energies for the three species are shown in Table 1.

Discussion

The geometries calculated for **11** and **13** are very similar to those calculated for their hydrocarbon counterparts. The largest difference between the calculated bond lengths in **11** and cyclopropanone (**17**) is the C2−C3 bond which is predicted to be 1.581 Å in **11** and 1.598 Å in cyclopropanone.[2a] This shortening is due to the two adjacent fluorine atoms which are known to shorten the proximal bonds in three membered-rings and to lengthen

(7) Edelson, S. S.; Turro, N. J. *J. Am. Chem. Soc.* **1970**, *92*, 2770.
(8) Sclove, D. B.; Pazos, J. F.; Camp, R. L.; Greene, F. D. *J. Am. Chem. Soc.* **1970**, *92*, 7488.
(9) Liberles, A.; Kang, S.; Greenberg, A. *J. Org. Chem.* **1973**, *38*, 1922.

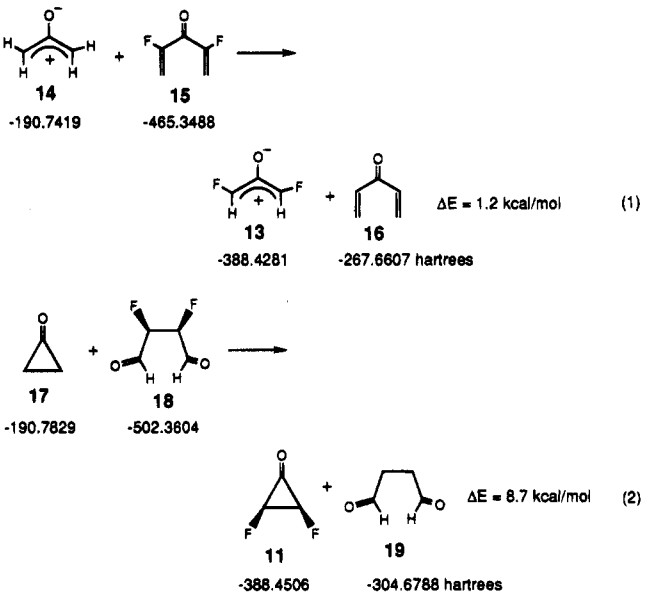
(10) The calculations employed Gaussian 94, revision B1: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Ragavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Forseman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andrew, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J., Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1995.
(11) McDouall, J. J.; Peasley, K.; Robb, M. A. *Chem. Phys. Lett.* **1988**, *148*, 183.

Table 1. Energies for 11–13 from CAS(4/4)/6-31G Calculations**

property	11	12	13
$-E$, hartrees	388.450 62	388.425 20	388.428 07
$-E$(CASPT2N), hartrees	389.272 43	389.250 17	389.254 15
ZPE, kcal/mol	31.4	30.0	29.4
ΔE, kcal/mol	0.0	14.5	12.1
ΔE(CASPT2N), kcal/mol	0.0	12.6	9.5

the distal one.[12] The only significant differences between the calculated structures for **13** and oxyallyl (**14**) are the C–C bonds which are shorter in **13** (1.446 Å) compared with oxyallyl (1.467 Å)[2a] and the CCC bond angle which is 108° in **13** and 114° in oxyallyl.[2a] In the transition structure for cyclopropanone going to oxyallyl,[2a] the dihedral angles measured as OCCH are −24° and −179° while the corresponding dihedral angles in **12** are OCCF = 19.1° and OCCH = −148°. The carbonyl carbon in transition structure **12** is more pyramidal (<$OC_1C_2C_3$ = −161°) than the corresponding carbon in the parent transition structure(<$OC_1C_2C_3$ = −171°). The CCC bond angle is predicted to be 110° in the parent transition structure while in **12** it is calculated to be 97°. Compared with the hydrocarbon system, transition structure **12** is not as close in structure to **13**. This is because the difference in energy calculated for cyclopropanone going to oxyallyl is greater (21.6 kcal/mol at the CAS(4/4)/6-31G* + ZPE level)[2a] than the difference between **11** and **13** (12.1 kcal/mol). According to the Hammond postulate a less endothermic reaction will resemble the product less than a similar, more endothermic one. The barrier for **11** going to **13** via transition structure **12** is calculated to be 14.5 kcal/mol at the CAS(4/4)/6-31G** level. The corresponding value calculated for cyclopropanone ring opening to oxyallyl is 21.6 kcal/mol.[2a] It is noteworthy that at the CASPT2N level the barrier for **11** going to **13** decreases to 12.6 kcal/mol while the barrier for the parent cyclopropanone undergoing ring opening increases to 28 kcal/mol.[2a] Thus, **11** is predicted to have about half the barrier for ring opening as does the cyclopropanone itself.

What is the reason for the lower barrier for ring opening of **11** compared to the parent cyclopropanone? Certainly, the less endothermic reaction of **11** going to **13** compared with **17** going to **14** is a major factor, but what is the origin for the lower value? In principle, it could be due to destabilization of the cyclopropanone system by fluorine, stabilization of oxyallyl by fluorine, or a combination of the two. To investigate this question, we have determined the reaction energies for reactions 1 and 2. The structures **15**, **16**, **18**, and **19** were determined at the geometry-optimized HF/6-31G** level, while the energies of **11**, **13**, **14**, and **17** made use of CAS(4/4)/6-31G** values. To a first approximation, reaction 1 will yield the difference in stability of the oxyallyl system due to fluorine substitution. Analogously, reaction 2 will yield the difference in stability of the cyclopropanone system due to substitution by vicinal fluorine atoms. The energy of reaction 1 is 1.2 kcal/mol which implies that there is little difference in stability of the oxyallyls **13** and **14**. In reaction 2, the energy of reaction is 8.7 kcal/mol, suggesting that each fluorine atom destabilizes the cyclopropanone system by about 4 kcal/mol. This value is almost identical to the value suggested



by O'Neal and Benson[13] for the increase in strain energy of a cyclopropane per F substituent.[14] The energy change in reaction 2 (8.7 kcal/mol) is almost exactly the same as the difference (9.5 kcal/mol) between the stabilities of **14** and **17** (21.6 kcal/mol) and **11** and **13** (12.1 kcal/mol). Thus, the destabilization of cyclopropanone by fluorine accounts for the fact that **11** has a much lower barrier to ring opening than the parent system. This may be contrasted with the modest changes in reactivity of fluorinated versus nonfluorinated methylenecyclopropanes which undergo ring opening to trimethylenemethanes. In limited studies Dolbier and co-workers[15] have found that the activation enthalpies for ring opening of fluorinated methylenecyclopropanes are only slightly lowered compared with non fluorinated systems.

Summary and Conclusions

Difluorocyclopropenone (**5**) undergoes Diels–Alder reaction with 1,3-diphenylisobenzofuran (**2**) to produce an initial adduct (**6**) which was not detected. The presumed intermediate difluorocyclopropanone **6** undergoes further reaction with **2** most likely via oxyallyl **10** and produces two 1:2 adducts (**7** and **8**) in a 9:1 ratio. Ab initio calculations predict that *cis*-2,3-difluorocyclopropanone (**11**) should have a barrier to ring opening to the corresponding oxyallyl **13** about half as large as that of the parent cyclopropanone. This is consistent with the apparent high reactivity of the presumed intermediate cyclopropanone **6**. Calculations suggest that the increased reactivity of the fluorinated system is a consequence of the destabilization of the cyclopropanone **6** by the two fluorine substituents.

Experimental Section

Reaction of 1,3-Diphenylisobenzofuran (2) with Difluorocyclopropenone (5). A mixture of 60 mg (0.222 mmol) of diphenylisobenzofuran and 20 mg (0.222 mmol) of difluo-

(12) For a recent review of fluorinated cyclopropanes and their thermal rearrangments, see: Dolbier, W. R., Jr. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press. Ltd: Greenwich, CT, 1993; Vol. 3.

(13) O'Neal, H. E.; Benson, S. W. *J. Phys. Chem.* **1968**, *72*, 1866.

(14) For a discussion of the effects of fluorine substitution, see: Smart, B. E. in *Molecular Structure and Energetics*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: Deerfield Beach, FL, 1986; Vol. 3.

(15) (a) Dolbier, W. R., Jr.; Fielder, T. H., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 5577. (b) Dolbier, W. R., Jr.; Burkholder, C. R. *Tetrahedron Lett.* **1983**, *24*, 1217. (c) Reference 10.

rocyclopropenone was stirred in 2 mL of degassed methylene chloride at room temperature overnight. The solvent was removed under reduced pressure, and the solid products were purified by column chromatography on silica gel using gradient elution (starting with 100% hexane and working to 30% EtOAc/hexane). The product **7** was isolated as a white solid (30 mg, 43%). This product can be recrystallized from EtOAc: mp 196–198 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.7 (d, 4H), 7.5 (overlapping signals, 6H), 7.36 (dd, J = 5.6, 3.1 Hz, 2H), 7.32-7.24 (m, 10H), 7.20 (dd, J = 5.6, 3.0 Hz, 2H), 7.10 (dd, J = 5.6, 3.1Hz, 2H), 6.61 (dd, J = 5.4, 3.1 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 86.1 (d, J = 18.8 Hz), 92.3 (d, J = 24 Hz), 103.6 (d, J = 237.5 Hz), 122.7, 122.9, 125.8, 127.2, 127.3, 127.9, 127.9, 128.1, 129.1, 129.2, 134.1, 135.4, 143.5, 143.7, 190.1 (t, J = 40 Hz); ^{19}F NMR (200 MHz, $CDCl_3$) δ −165.7; MS (CI) m/e calcd for M + H 631.2085, found 631.2064.

The minor isomer **8** is fairly insoluble in EtOAc and can be filtered from the EtOAc solution before recrystallization: yield 4 mgs (6%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (t, J = 7.22 Hz, 4H), 7.12 (dd, J = 7.17, 7.72 Hz, 8H), 7.17 (dd, J = 7.18, 3.0 Hz, 4H), 7.38 (dd, J = 5.56, 3.10 Hz, 4H), 7.76 (d, J = 7.64 Hz, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 88.6 (d, J = 20.4 Hz), 103.1 (d, J = 235.4 Hz), 122.7, 126.3, 127.7, 128.7, 134.6, 144.8, 144.8, 194 (t); ^{19}F NMR (200 MHz, CD_3CN) δ −178.5; MS m/e (EI) calcd 630.2006, found 630.2031.

Acknowledgment. We thank the National Science Foundation for financial support, and W.P.D. thanks the Alfred P. Sloan Foundation for a research fellowship (1990–1994).

JO9511713