Pergamon

Tetrahedron Letters, Vol. 35, No. 9, pp. 1357-1360, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0032-S

Attempted Preparation of 5,5-Difluoro-1,4-diphenylbicyclo[2.1.0]pentane Serendipitous Synthesis of 1,3-Difluoro-2,4-diphenylbenzene

Scott B. Lewis and Weston Thatcher Borden*

Department of Chemistry, University of Washington, Seattle, WA 98195

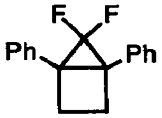
Abstract: Addition of difluorocarbene to 1,2-diphenylcyclobutene, using $PhHgCF_3$, results in formation of 1,3-difluoro-2,4-diphenylbenzene. A mechanism for this reaction is proposed.

Bicyclo[2.1.0]pentane (**1**) is known to release ca. 50 kcal/mol of strain energy upon homolysis of the bridgehead bond to produce 1,3-cyclopentanediyl.[1] Consequently $\Delta H^{\ddagger}$ for bridge flipping in **1** is only 36.8 kcal/mol.[2] Introduction of phenyl rings at C_1 and C_4 of **1** further reduces the barrier to bridge flipping to a value of 12 kcal/mol in **2**.[3]

It has been well documented, both experimentally[4] and computationally,[5] that *geminal* fluorines on a cyclopropane ring weaken the distal ring bond by >9 kcal/mol. Therefore, we undertook the synthesis of 5,5-difluoro-1,4-diphenylbicyclo[2.1.0]pentane (**3**) in the hope of preparing a derivative of **1** in which the bond between the bridgehead carbons would have a dissociation energy of close to zero.

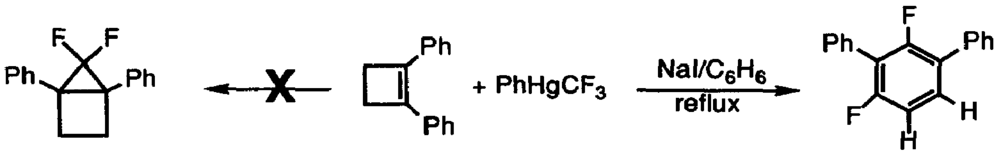
1

2



3

1,2-Diphenylcyclobutene (**4**) was prepared by intramolecular McMurry coupling of dibenzoylethane,[6] using $TiCl_3$/LAH in THF.[7] Attempts to add difluorocarbene to **4**, employing CF_2Br_2/Zn in THF,[8] failed to produce any adduct. Generation of CF_2 from excess $PhHgCF_3$[9] in the presence of **4** produced, in 77% isolated yield, a single adduct, m.p. 73-74° C after recrystallization from ethanol. However, the adduct was clearly not **3** but was, instead, identified as 1,3-difluoro-2,4-diphenylbenzene (**5**).



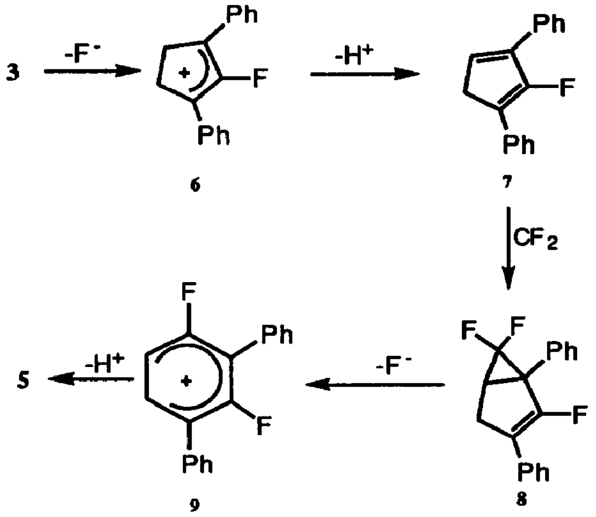
3 **4** **5**

The formula of the adduct was established as that of **4** + $2CF_2$ - 2HF by high-resolution mass spectroscopy (calc. for $C_{18}H_{12}F_2$: 266.0907, found: 266.0895). The 300 MHz ^1H NMR spectrum ($CDCl_3$) showed eleven aromatic protons in the region δ 7.56 - 7.34 and a twelfth at δ 7.06 (td, 1H, J = 8.4 and 1.4 Hz). The 188 MHz ^{19}F NMR spectrum revealed two non-equivalent fluorines as multiplets centered at δ 37.40 and 34.77 (relative to CF_3CO_2H at δ 77.0). Proton decoupling experiments showed the proton at δ 7.06 to be coupled to the downfield fluorine and to another proton, both with J = 8.4 Hz. Decoupling all of the protons simplified the ^{19}F spectrum to two doublets with J = 8.0 Hz. The ^1H and ^{19}F NMR data indicate that the fluorines are *meta* to each other and that the proton at δ 7.06 is *ortho* to the fluorine at δ 37.40 and to another proton, thus implying stucture **5**.

This structural assignment is supported by the 75 MHz, proton-decoupled, ^{13}C NMR spectrum ($CDCl_3$) δ 159.30 (dd, $^1J_{CF}$ = 248.9, $^3J_{CF}$ = 7.0 Hz), 156.60 (dd, $^1J_{CF}$ = 250.1, $^3J_{CF}$ = 7.0 Hz), 135.30, 130.37, 130.34, 129.93, 129.77 (t, $^3J_{CF}$ = 4.5 Hz), 129.34, 129.08, 129.01, 128.52, 128.27, 127.72, 125.67 (dd, $^2J_{CF}$ = 14.9, $^4J_{CF}$ = 3.8 Hz), 118.78 (t, $^2J_{CF}$ = 18.0 Hz), 111.69 (dd, $^2J_{CF}$ = 23.18, $^4J_{CF}$ = 3.7 Hz). The appearance of the ^{13}C resonance at δ 118.78 as a triplet with J_{CF} = 18.0 Hz indicates that this carbon is *ortho* to both fluorines, and its absence from the DEPT 135 spectrum shows that it bears a phenyl group. Of the two other carbons that have two-bond C-F coupling constants, the one at δ 125.67 is shown by the DEPT 135 spectrum to be attached to a phenyl group and the one at δ 111.69 to be attached to a proton. The DEPT 135 spectrum also shows that the carbon at δ 129.77, which exhibits equal coupling constants to the two fluorines *meta* to it, bears a proton.

The mechanism for formation of **5** presumably involves the intermediacy of **3**. Ring opening in **3**, either accompanied or followed by loss of fluoride ion, forms **6** and then, after proton, loss **7**. Addition of a second mole of CF_2 to the less substituted double bond of **7** leads to **8**.[10] Loss of fluoride ion from **8**, concomitant with ring opening, forms **9**, which loses a proton to give **5**.[11]

Attempts to isolate the putative intermediate, 1,3-diphenyl-2-fluoro-1,3-cyclopentadiene (**7**) were unsuccessful. When the reaction of **4** was performed with only 0.5 equivalents of $PhHgCF_3$, in addition to large amounts of unreacted **4**, the only isolable product was again **5**. Apparently, the C_3-C_4 double bond in **7** is considerably more reactive toward CF_2 than the sterically more encumbered double bond in **4**. Consequently, even at low concentrations, **7** competes very effectively with **4** for CF_2.



The attempted preparation of 3 reported here provides, serendipitously, a regiospecific synthesis of a tetrasubstituted benzene derivative that would be difficult to prepare by a more conventional route. Additional attempts to generate 3, under conditions where it can be isolated, are in progress.

Acknowledgment. We thank the National Science Foundation for support of this research.

References

1. Wiberg, K. B. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 312.
2. Baldwin, J. E.; Ollerenshaw, J. *J. Org. Chem.* **1981**, *46*, 2116.
3. Dougherty, D. A.; Coms, F. D. *J. Am. Chem. Soc.* **1989**, *111*, 6894.
4. (a) Dolbier, W. R. *Acc. Chem. Res.*, **1981**, *14* (7), 195. (b) Roth, W. R.; Kirmse, W.; Hoffmann, W.; Lennartz, H. W. *Chem. Ber.* **1982**, *115*, 2508. (c) Smart, B. E. In *Molecular Structure and Energetics;* Liebman, J. F.; Greenberg, A., Eds.; VCH Inc.: Deerfield Beach, Fl, 1986; Vol 3, p. 141.
5. (a) Greenberg, A.; Liebman, J.; Dolbier, W. R., Jr.; Medinger, K. S.; Skaneke, A. *Tetrahedron* **1983**, *39*, 1533. (b) Getty, S. J.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.* in press; (c) Xu, J. D.; Hrovat, D. A.; Borden, W. T. *J. Am. Chem. Soc.*, submitted for publication.

6. Bailey, P. S.; Robert, L. E. *J. Am. Chem. Soc.* **1948**, *70*, 2412.
7. Baumstark, A. L.; Bechara, E. S. H.; Semigran, M. J. *Tetrahedron Lett.* **1976**, *37*, 3265.
8. Dolbier, W. R.; Wojtowicz, H.; Burkholder, C. R. *J. Org. Chem.* **1990**, *55*, 5420.
9. Seyferth, D.; Hopper, S. P. *J. Org. Chem.* **1972**, *37*, 4070.
10. A preference for the addition of CF_2 to the less substituted of the two double bonds in 1,3-pentadiene has also been reported. Dolbier, W. R.; Sellers, S. *J. Am. Chem. Soc.*, **1982**, *104*, 2494. The regiochemical preference of both CF_2 addition reactions for the less substituted of the two double bonds almost certainly has an electronic component and is not due to just a steric effect.
11. Aromatization of the CF_2 adduct of indene by a similar mechanism has been reported. Dolbier, W. R. Jr.; Keaffaber, J. J.; Burkholder, C. R.; Koroniak, H.; Pradhan, J. *Tetrahedron*, **1992**, *48*, 9649.

(*Received in USA* 16 *November* 1993; *revised* 15 *December* 1993; *accepted* 22 *December* 1993)