## SELENOFLUORENONE: SYNTHESIS AND CYCLOADDITION CHEMISTRY

## Peter T. Meinke, Grant A. Krafft\*, and James T. Spencer Department of Chemistry, Syracuse University Syracuse, New York 13244-1200

Summary: Selenofluorenone, prepared from fluorenyl selenocyanate by base-induced elimination, participates efficiently in Diels-Alder cycloaddition and 1,3-dipolar cycloaddition reactions.

Significant interest in the chemistry of highly reactive carbon-heteroatom double bonds has developed over the past decade. Notable accomplishments include the synthesis of carbon-silicon double bonds by West and Michl,<sup>1a</sup> T. J. Barton,<sup>1b</sup> and others, and the synthesis of carbon-sulfur double bonds in thioaldehydes by Vedejs<sup>2</sup> and others.<sup>3</sup> Selenium-carbon double bonds also have attracted attention, with the first synthesis of sterically hindered selenoketones by D. H. R. Barton<sup>4</sup> and Guziec<sup>5</sup>, and more recently with the synthesis of highly reactive selenoaldehydes by us.<sup>6</sup> In this Letter we describe the simple and efficient synthesis of selenofluorenone (1), and its cycloaddition reactions with dienes and dipoles.

The synthesis and cycloaddition reactions of selenofluorenone proceed readily in two steps from fluorenyl bromide as illustrated below. Treatment of fluorenyl bromide<sup>7</sup> with potassium selenocyanate in refluxing THF produces fluorenyl selenocyanate in 90% yield, which is converted to selenofluorenone upon syringe pump addition of Et<sub>3</sub>N in CH<sub>2</sub>Cl<sub>2</sub>/THF over 2-8 hours at 25°C.<sup>8</sup> Selenofluorenone generation occurs in the presence of diene or dipole reactants, resulting in rapid and efficient trapping via cycloaddition reaction.<sup>9</sup> Table I outlines the results of these cycloaddition reactions.<sup>10</sup>



In all instances, the generation and cycloaddition reactions of selenofluorenone proceeded with high efficiency (82-98% yields). Excellent cycloaddition regioselectivity also was observed, with formation of a single isomer (> 50:1) in reactions with 1-substituted dienes, and mixtures of regioisomers (7:3 to 5:1) in reactions with 2-substituted dienes. The regiochemical results in the Diels-Alder reactions are consistent with a frontier molecular orbital interpretation<sup>11</sup> involving predominant transition state interactions between the LUMO of selenofluorenone (large coefficient on selenium) and the HOMO of the diene. The regiochemical influence of the fluorenyl ring system is similar to the influence of electron withdrawing substituents, rather than conjugating substituents,<sup>12</sup> due to the stability of the aromatic fluorenyl carbanion.

Entry	Diene	Adduct(s)	Yield (%)
1		Se	98
2	$\checkmark$	Se Se	93
3		7 : 3 Se ,	82
4	$\succ$	Se	96
5		Se 	93
6	OR R = Et, TBS	$Se \rightarrow OR \qquad Se \rightarrow OR$ $R = TBS \qquad 5 \qquad : \qquad 1$ $R = Et \qquad 4 \qquad : \qquad 1$	91 94
7		Se O Se O Me	93
8	CO2Et	Se Se CO <sub>2</sub> Et	88
9	$\hat{\mathbf{O}}$	Se	97
10	OTBS	Se- OTBS	91

**Table I.** Diels-Alder cycloaddition reactions of selenofluorenone.

The determination of cycloadduct regiochemistry was accomplished by a combination of several methods, including extensive NOE experiments, chemical modification and single crystal X-ray diffraction. For adducts of C-1 substituted dienes, NOE experiments indicated significant enhancement (10-15%) of the C-3' methine proton



resonances and the resonances of protons attached to the C-3' substituent. Only small (< 3%) or no enhancement was observed for the C-6' methylene resonances in these adducts.<sup>13</sup> Corroboration of NOE interpretations was obtained by reductive deselenation and olefin hydrogenation, as illustrated above for conversion of the *trans*-2-methylpentadiene adduct 2 to 2-fluorenyl-4-methylpentane, 3, which was identified by NMR and mass spectral data. For enol ether adducts of 2-siloxy or 2-alkoxy substitued dienes, hydrolysis and separation provided isomeric tetrahydroselenapyrones which were easily identifiable by their NMR spectra.

Selenofluorenone also reacted with dipolar reagents, though in only one reaction, involving 2,4,6trimethylbenzonitrile-N-oxide, could a cycloadduct 4 be isolated. Several other dipoles (e.g. nitrones, ethyl diazoacetate, stabilized azomethine ylides) reacted, but no isolable cycloadducts could be obtained from multicomponent reaction mixtures.<sup>14</sup> <sup>13</sup>C-NMR data permitted tentative regiochemical assignment of the nitrile oxide cycloadduct. A single crystal X-ray analysis provided unambiguous confirmation of the structure as the 1',4',2'-oxaselenazole 4 (Figure 1).<sup>15</sup> This result is not consistent with the FMO interpretation discussed above which would have predicted reversed regiochemistry. However, the regiochemistry observed here may be the result of predominant steric inter-

actions between the fluorenyl ring and the aryl group, destabilizing the transition state leading to the expected regioisomeric isoxaselenazole.<sup>16</sup>





Figure 1. PLUTO representation of 4.

Pyridine N-oxide did not undergo 1,3-dipolar cycloaddition, however. In this instance a 25-30% yield of a dimeric selenofluorenone adduct 5 was isolated. This structure was determined by NMR, mass spectral data and reductive deselenation, which afforded the known 9,1'-bifluorenyl. This selenofluorenone dimer also had been observed in several Diels-Alder reactions, though only in trace quantities (2-10%).<sup>17</sup>

The cycloaddition reactions of selenofluorenone described in this Letter represent the first such examples involving selenoketones, and provide insight into structural and electronic characteristics of the selenium-carbon double bond. Efforts to explore the chemistry of selenocarbonyl adducts and to expand the scope of selenocarbonyl reactivity are continuing in our laboratories.



Acknowledgments. This work was supported by a grant from the National Science Foundation. Acquisition of the X-ray diffractometer was made possible by an instrumentation grant from the National Science Foundation. GAK has been a fellow of the American Cancer Society, 1983-1986.

## **REFERENCES AND NOTES**

- 1. a. Drahnak, T. J., Michl, J., West, R. J. Am. Chem. Soc. 1981, 103, 1845-1846; b. Barton, T. J., Burns, G. T., Tetrahedron Letters 1983, 24, 159-163, and references therein.
- 2. a. Vedejs, E., Eberlein, T. H., Varie, D. L. J. Am. Chem. Soc. 1982, 104, 1445-1446; b. Vedejs, E., Perry, a. Vedejs, E., Eberlein, T. H., Vanc, D. L. J. Am. Chem. Soc. 1962, <u>104</u>, 1449-1440, U. Vedejs, E., Ferry, D. A. J. Am. Chem. Soc., 1983, <u>105</u>, 1683-1685; c. Vedejs, E., Perry, D. A., Houk, K. N., Rondan, N. G. J. Am. Chem. Soc. 1983, <u>105</u>, 6999-7001; d. Vedejs, E., Wilde, R. G. J. Org. Chem. 1986, <u>51</u>, 117-119; e. Vedejs, E., Eberlein, T. H., Mazur, D. J., McClure, C. K., Perry, D. A., Ruggeri, R., Schwartz, E., Stults, J. S., Varie, D. L., Wilde, R. G. and Wittenberger, S. J. Org. Chem. 1986, <u>51</u>, 1556-1562.
   Kraff, G. A., Meinke, P. T. Tetrahedron Letters 1985, <u>26</u>, 1947-1950; Kirby, G. W., Lockhead, A. W., Edeland, C. M. J. Chem. Soc. Chem. Chem. Soc. 1985, <u>26</u>, 1947-1950; Kirby, G. W., Lockhead, A. W., Edeland, C. M. J. Chem. Soc. Chem. Chem. 1986, <u>51</u>, 1566-1562.
- and Sheldrake, G. N. J. Chem. Soc., Chem Commun. 1984, 922-924, and refrences therein; Baldwin, J. E., Lopez, R. C. G. Tetrahedron 1983, 39, 1487-1498.
- 4. Back, T. G., Barton, D. H. R., Britten-Kelley, M. R., Guziec, Jr., F. S. J. Chem. Soc., Perkin Trans. I. 1976, 19, 2079-2084.
- 5. Guziec, Jr., F. S., Moustakis, C. A. J. Org. Chem. 1984, 49, 189-191, and references therein.
- 6. Krafft, G. A., Meinke, P. T. J. Am. Chem. Soc. 1986, 108, 1314-1315.
- Wragg, A. H., Stevens, T. S., and Ostle, D. M. J. Chem. Soc. 1958, 4057-4064. 7.
- 8. Ethyl selenoglyoxalate has been prepared and trapped with cyclopentadiene in modest yield from ethyl selenocyanatoacetate by treatment with Et3N in refluxing EtOH. Kirby, G. W., Trethewey, A. N. J. Chem. Soc., Chem Commun. 1986, 1152-1154.
- The following experimental procedure for generation and trapping of selenofluorenones is typical. Ethyl 3',6'-dihydro-6'-methyl-spiro[9H-fluorene-9,2'-[2'H]selenapyran]-3'-carboxylate. To 10 9. mL of a dichloromethane solution containing 200 mg (0.74 mmol) 9-selenocyanatofluorene and 100 mg (1.48 mmol) ethyl sorbate was added a THF solution (10 mL) containing 207 µL (1.48 mmol) Et<sub>3</sub>N via syringe pump over 6.5 h at 25°C. The reaction mixture was diluted to 50 mL with pentane and filtered through a 4 cm column of neutral alumina. The filtrate was concentrated under reduced pressure and purified by flash chromatography on silica gel using 25:1:1 hexane: Et<sub>2</sub>O:CH<sub>2</sub>Cl<sub>2</sub> as the eluting solvent, to yield 125 mg (88%) of the desired adduct.
- 10. Yields correspond to isolated material, chromatographically purified to homogeneity. All adducts exhibited satisfactory spectral data (<sup>1</sup>H and <sup>13</sup>C APT NMR, IR, and mass spec).
- 11. Fukui, K. Angew. Chem., Int. Ed. Engl. 1982, 21, 801-809, and references therein.
- 12. Selenoaldehydes with electron withdrawing substituents exhibit similar regioselectivity. With conjugating substituents, opposite regioselectivity is observed. Meinke, P. T. and Krafft, G. A., Manuscript in preparation.
- 13. The NOE experiments on all adducts revealed qualitatively consistent enhancements in the proton resonances at C-3' upon irradiation of aromatic proton resonances, as illustrated for the 2-methylpentadiene adduct, 6:
- 14. Attempts to isolate adducts of these dipoles and electron poor selenoaldehydes also have been unsuccessful, presumably due to product instability. (Unpublished results.) Similar instabilities have been noted for certain dipolar adducts of thioaldehydes. (Ref. 2c).
- 15. X-ray analysis: Crystallized in monoclinic system, P21/c (#14) space group. Data collected at 23°C on a Rigaku AFC5S diffractometer (Mo K-α



radiation,  $2\theta(\max) = 49.1 \text{ deg}$ ). 1409 observed reflections yielded lattice **6** parameters of a = 10.447(3) Å, b = 10.971(6) Å, c = 16.502(3) Å, ß = 99.03(2) deg with cell vol. = 1868(1) Å<sup>3</sup>, 4 molecules per unit cell. Full matrix solution refined to yield residuals of R = 0.036 and R<sub>w</sub> = 0.046. Full crystallographic data submitted to Acta Cryst.

- 16. Steric effects are significant for aryl nitrile-N-oxide cycloadditions. For example, regioselectivities for benzonitrile-N-oxide and 2,4,6-trimethylbenzonitrile-N-oxide reverse when the dipolarophile reactant changes from ethyl acrylate to ethyl crotonate. Sasaki, T., Eguchi, S., Tanaka, Y. Tetrahedron 1980, 36, 1565-1572; Christl, M., Huisgen, R. Chem. Ber. 1973, 106, 3345-3367; Huisgen, R., Sustmann, R., Wallbillich, G. Chem. Ber. 1967, 100, 1786-1801.
- 17. The analogous dimer from thiofluorenone also has been reported. The postulated mechanism involved fluorenyl disulfide diradical formation via head-to-head coupling, six-membered ring formation and rearomatization. Schonberg, A., Brosowski, K.-H., Singer, E. Chem. Ber. 1962, 95, 1910-1914.

(Received in USA 24 April 1987)