atmosphere of nitrogen. Workup of the reaction mixture followed by column chromatography (7:4 hexane–ethyl acetate) gave 2.86 g (68%) of racemic **13**. To a solution of 2.51 g (9 mmol) of racemic **13** in 10 mL of ethyl acetate was added 1.10 g (9.1 mmol) of (+)-α-methylbenzylamine, and the resulting solution was stirred for 10 min at room temperature. After addition of 100 mL of ether, the mixture was cooled with a dry ice/acetone bath. The precipitates were collected, washed with ether, and dried to give 3.33 g (93%) of the salt **16**. Recrystallization of this salt (2.44 g) from ethyl acetate gave 0.46 g of crystals, which were, according to Field,[1e] mainly composed of (*S*)-**13**. Treatment of the crystals with a mixture of 30 mL of 5% aqueous $KHSO_4$ and 30 mL of ethyl acetate for 10 min gave, after workup, 0.28 g of **13** with $[\alpha]_D$ −8.3° (*c* 1.042, benzene). Therefore, (−)-**13** was concluded to have an *S* configuration. From the mother liquor of recrystallization was recovered 1.21 g of **13** with $[\alpha]_D$ +2.1° (*c* 1.045, benzene) by treating it with 20 mL of 5% aqueous $KHSO_4$ for 10 min.

Acknowledgment. We thank Dr. G. F. Field of the Research Division, Hoffmann-La Roche Inc., for helpful suggestions.

Registry No. **1**, 68-11-1; **2**, 102-96-5; (+)-**3**, 76665-77-5; (−)-**3**, 76665-78-6; (+)-**3** acid chloride, 76665-79-7; (−)-**3** acid chloride, 76665-80-0; **4**, 76741-87-2; **5** (isomer 1), 76665-81-1; **5** (isomer 2), 76665-82-2; **6**, 2365-48-2; (+)-**7**, 76665-83-3; **8**, 3316-24-3; **9**, 705-60-2; **10**, 61379-36-0; (+)-**11**, 76665-84-4; (−)-**11**, 76665-85-5; **12**, 76665-86-6; (±)-**13**, 61379-25-7; (*R*)-**13**, 61379-30-4; (*S*)-**13**, 69088-64-8; (+)-**14**, 76665-87-7; **15**, 76665-88-8; (*S*)-**16**, 69088-65-9; **17** (isomer 1), 76665-89-9; **17** (isomer 2), 76665-90-2; L-phenylalanine methyl ester HCl, 7524-50-7.

1-Thio-Substituted Cyclopropylphosphonium Salts: Reagents for Pentannulation Reactions

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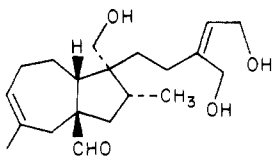
Received September 9, 1980

The preparation and pentannulation reactions of 1-(phenylthio)-, 1-(methylthio)- and 1-(isopropylthio)-cyclopropylphosphonium fluoborates are described. As part of a synthetic approach to portulal, a plant-growth regulator, 2-(carbomethoxy)-4-methylcyclohept-4-en-1-one is converted to its bicyclo[5.3.0]decenone derivative. This annulation reaction illustrates the synthetic application and limitations of the 1-thio-substituted cyclopropylphosphonium reagents.

In conjunction with the synthesis of hydroazulene natural products such as portulal,[1] **1**, we have been interested



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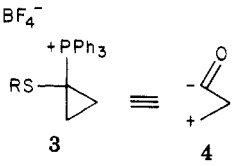
in the efficient annulation of cyclopentanone ring systems that bear a functionalized carbon atom at the bridgehead position. Methodology for the one-step annulation of β-keto esters[2] to cyclopentanone precursors was lacking prior to our study. Ring-fused cyclopentanones **2** can be valuable precursors for further elaboration to natural products by α-alkylation and/or geminal functionalization as outlined in Scheme I.

Our design of a three-carbon synthon of structure **3** that is equivalent to a cyclopropane zwitterion **4** was based on (1) the facile ring opening of activated cyclopropanes by nucleophiles[3] and (2) an umpolung reactivity[4] for an incipient acyl anion equivalent.



In a preliminary report,[5] we have described 1-(phenylthio)cyclopropylphosphonium fluoborate as an efficient pentannulation reagent. In one step, reagent **3** (R = Ph) reacts with enolates of β-keto esters to form 1-(phenylthio)cyclopentenes in good to high yield. The vinyl sulfide products were then hydrolyzed to the β-carboxycyclopentanones with hydrochloric acid (Scheme II). Since none of the milder mercury-catalyzed methods for hydrolysis of vinyl sulfides[6] were effective and only HCl hydrolysis of aryl vinyl sulfides worked in our hands, we sought new reagents of **3** in which R was an alkyl group. Alkyl vinyl sulfides are usually hydrolyzed to ketones under milder conditions.

In this report, we describe the preparation of 1-methylthio (**3b**) and 1-isopropylthio (**3c**) derivatives of **3**

(1) (a) Yamazaki, S.; Tamura, S.; Marumo, F.; Saito, Y. *Tetrahedron Lett.* **1969**, 359. (b) Matsahashi, M.; Shibaoka, H. *Plant Cell Physiol. Jpn.* **1965**, *6*, 87. (c) Tokoroyama, T.; Matsuo, K.; Kanazawa, R.; Kotsuki, H.; Kubota, T. *Tetrahedron Lett.* **1974**, 3093. (d) Kanazaw, R.; Kotsuki, H.; Tokoroyama, T. *Ibid.* **1975**, 3651.

(2) Recently, a number of efficient methods for the preparation of 3,4-annulated cyclopentanones have been reported. See: (a) Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699 and references therein. Other methodology leading to annulated cyclopentanes via intramolecular Wittig cyclization includes: (b) Fuchs, P. *J. Am. Chem. Soc.* **1974**, *96*, 1607; (c) Dauben, W. G.; Hart, D. J. *Ibid.* **1975**, *97*, 1622.

(3) Danishefsky, S.; Dynak, J.; Hatch, E.; Yamamoto, M. *J. Am. Chem. Soc.* **1974**, *96*, 1256. References 2b and 2c.

(4) Grobel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.

(5) Marino, J. P.; Landick, R. *Tetrahedron Lett.* **1975**, 4531.

(6) (a) Corey, E. J.; Shulman, J. *J. Org. Chem.* **1970**, *35*, 777. (b) Corey, E. J.; Erickson, B. W.; Noyori, R. *J. Am. Chem. Soc.* **1971**, *93*, 1724. (c) Carlson, R. G.; Mardis, W. S. *Ibid.* **1975**, *40*, 817. (d) Mukaiyama, T.; Narasaka, S.; Furwato, M. *J. Am. Chem. Soc.* **1972**, *94*, 8641. (e) Cohen, T.; Bennett, D. A.; Mura, A. J., Jr.; *J. Org. Chem.* **1976**, *41*, 2506. (f) Bestmann, H. J.; Angerer, J. *Tetrahedron Lett.* **1969**, 3665. (g) Mura, A. J., Jr.; Majetich, G.; Grieco, P. A.; Cohen, T. *Ibid.* **1975**, 4437. (h) Trost, B. M.; Stanton, J. L. *J. Am. Chem. Soc.* **1975**, *97*, 4018.

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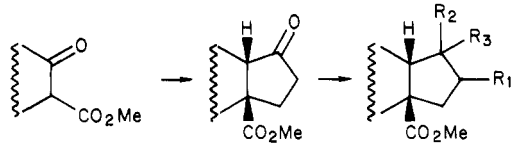
Scheme I



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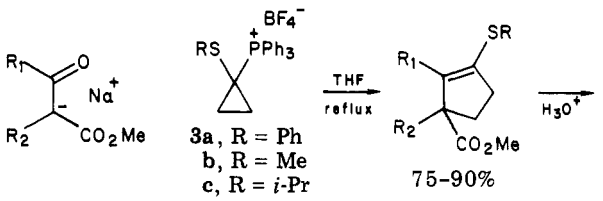
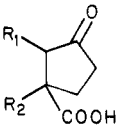
Scheme II



3a, R = Ph
b, R = Me
c, R = *i*-Pr

75–90%

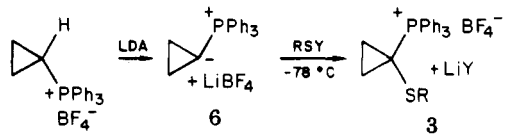


>90%

and their reactions with various enolates of 2-(carbomethoxy)-4-methylcyclohept-4-en-1-one. We shall also report a mild method for hydrolysis of an isopropyl vinyl sulfide to a cyclopentanone system.

The preparation of the 1-thio-substituted cyclopropylphosphonium fluoborates is conveniently accomplished by the sulfenylation of triphenylphosphonium cyclopropylides. Because of the hygroscopic nature of cyclopropylphosphonium bromide,[7] it is preferable to work with the fluoborate salt. This salt may be prepared in 93% yield by dissolution of the bromide and excess sodium fluoborate in aq. methanol. Extraction of the methanolic solution with chloroform and evaporation of the dried chloroform solution yields pure cyclopropyl triphenylphosphonium fluoborate.

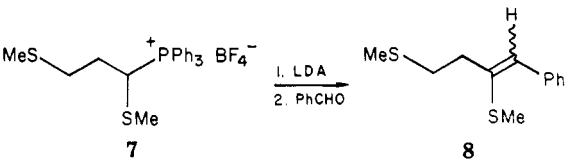
The cyclopropyl ylide is formed at −30 °C in tetrahydrofuran with 1 equiv of lithium diisopropylamide. Sulfenylation of the triphenylphosphonium cyclopropylide occurs cleanly at −30 °C with *N*-(phenylthio)succinimide[8] (to give **3a**), methyl disulfide (to give **3b**), and isopropyl disulfide (to give **3c**).



5 6 3

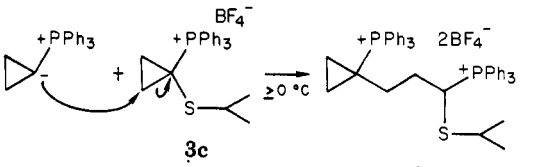
Y = SR or succinimide

Unexpectedly, the use of phenyl disulfide as a sulfenylating agent failed to yield any of reagent **3a**. Instead, it appears that as **3a** was formed in the sulfenylating reaction, the phenylthiolate anion generated from phenyl disulfide attacked the cyclopropane ring of **3a**, even at −30 °C. This was confirmed when significant amounts (>50%) of a ring-opened product (**7**) were isolated with the methyl disulfide reaction at 0 °C. The structure of **7** was confirmed by spectral analysis, and its conversion to an ylide that produced the Wittig product **8** with benzaldehyde. This last side reaction emphasizes the susceptibility of



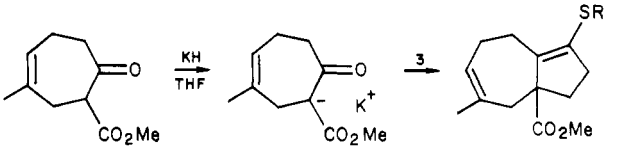
7 8

reagent **3a** to nucleophilic attack and the necessity for working at low temperatures. If the reaction temperature went above 0 °C, another side reaction that occurred during the preparation of **3c** is the ring opening of **3c** with the ylide **6**. The alkylated cyclopropyl bis(phosphonium salt) **9** was isolated in variable yields, depending on the temperature of the sulfenylation reaction. At 0 °C, 10% **9** was isolated; at room temperature, **9** was the major product.



3c 9

The pentannulation reactions with reagents **3a–c** were evaluated on 2-(carbomethoxy)-4-methylcyclohept-4-enone,[9] **10**, a precursor for a synthesis of portulal, **1**. The sodium enolate of β-keto ester **10** was treated with the 1-phenylthio reagent **3a** in a number of solvents (chloroform, tetrahydrofuran, benzene, and ether), with and without hexamethylphosphorous triamide. While the fluoborate salts **3** were not completely soluble in tetrahydrofuran, this solvent appeared to give the highest yields. The presence of hexamethylphosphorous triamide did not increase the yields or decrease reaction times at all.



10

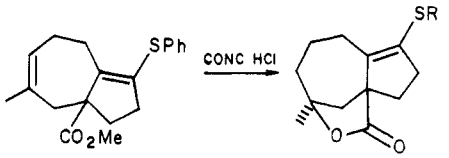
11a, R = Ph
b, R = Me
c, R = *i*-Pr

Reaction times for the annulations with all three reagents (**3a–c**) did not vary much, and maximum yields were obtained after 3 days of reflux in tetrahydrofuran. A comparison of various metal cations (Li, Na, K, Tl) of the enolate revealed a number of significant differences. Potassium enolates (from KH) reacted more readily and gave higher yields than sodium enolates (from NaH). Lithium enolates (from *n*-BuLi) and thallium enolates (from TlOEt) were ineffective in ring opening the cyclopropyl reagents **3**. In the case of lithium, no annulated product could be isolated, while only transesterification of the β-keto ester **10** occurred with thallium ethoxide. Cyclopropyl phenyl sulfide was a side product in the reaction of **3a** with the sodium enolate of **10**; this side product was not detected in the reactions of potassium enolates. An optimized set of reaction conditions for the preparation of **11a** (90% yield) consisted of refluxing the potassium enolate of **10** with reagent **3a** for 3 days.

Although the yield of annulated product, **11a**, was high (90%) for the 1-phenylthio reagent **3a**, the difficulty en-

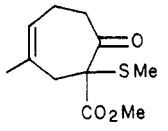
(7) Cyclopropylphosphonium bromide is commercially available from Aldrich or can be prepared by Schweizer's procedure: *J. Org. Chem.* **1968**, *33*, 336.
(8) Buchel, K. H.; Conte, A. *Chem. Ber.* **1967**, *106*, 1248.
(9) Prepared via a divinylcyclopropane route: Marino, J. P.; Ferro, M. P. *J. Org. Chem.*, companion paper in this issue. Recently reference to this compound was made in: Trost, B. M.; Runge, T. A.; Jungheim, L. N. *J. Am. Chem. Soc.* **1980**, *102*, 2840.

countered in the hydrolysis of phenyl vinyl sulfides preempted its use as the reagent of choice. Because the intermediate **11a** contains another trisubstituted double bond, mild hydrolysis of a vinyl sulfide to a ketone was critical. After many attempts at the hydrolysis of **11a**, the sole product from acid-catalyzed reactions was the lactonized vinyl sulfide **12**. Further treatment of **12** with refluxing concentrated hydrochloric acid did not produce any keto lactone.



11a 12

Clearly, the presence of other functional groups in a molecule that requires strong acid hydrolysis of the vinyl sulfide is undesirable. Thus, we turned to alkylthio-substituted reagents, since the vinyl sulfide products were expected to undergo hydrolysis under milder conditions. Both the 1-methylthio reagent **3b** and the 1-isopropylthio reagent **3c** reacted to form pentannulated products, as we anticipated. In the case of **3c**, the yields were 80–90%. However, a serious side reaction developed in the reactions of the 1-methylthio reagent, **3b**. In addition to 50% of the desired product **11b**, a 40% yield of 2-(carbomethoxy)-2-(methylthio)-4-methylcyclohept-4-enone, **13**, was isolated.

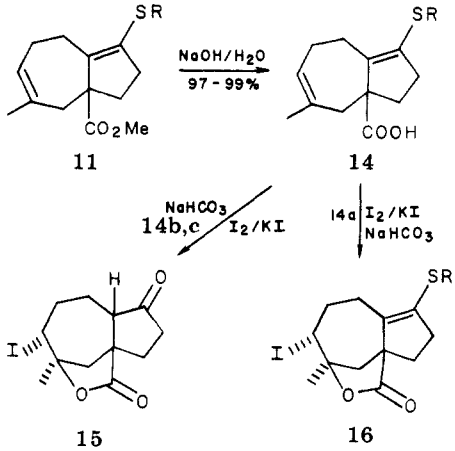


13

It appears that the enolate of the β-keto ester undergoes sulfenylation by the 1-methylthio reagent, **3b**. No such sulfenylation reaction was observed in the reactions of 1-(isopropylthio)cyclopropylphosphonium fluoborate **3c**.

Hydrolysis of the pentannulated products **11b** and **11c** to the corresponding cyclopentanones could still not be effected selectively. In numerous attempts, using mercuric ion catalysis or acid, hydrolyses yielded mixtures of ketones, keto lactones, and products arising from reactions of the isolated double bond.

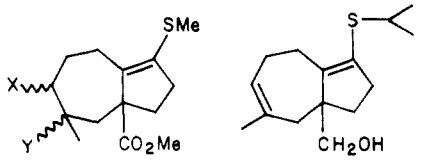
In an effort to use the propensity for lactonization to good advantage synthetically, the (alkylthio)cyclopentenes, **11b** and **11c**, were subjected to iodolactonization conditions. When the esters **11b** and **11c** were first hydrolyzed in base, a 97% yield of the corresponding angular carboxylic acids, **14b** and **14c**, were produced. Treatment of



11 14 15 16

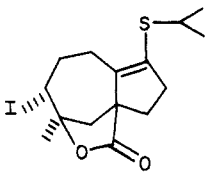
these acids with excess iodine/potassium iodide resulted in the formation of the keto iodo lactone[10] **15** (55%). The overall yield of the keto lactone **15** from the isopropyl reagent **3c** was 50%. The carboxylic acid **14a** from the 1-phenylthio reagent stopped at the iodo lactone, **16**, stage under the same reaction conditions. Once again, the phenyl vinyl sulfide proved to be resistant to hydrolysis.

When ester **11b** was subjected to iodolactonization conditions, no hydrolysis of the vinyl sulfide functionality was observed; instead a mixture of iodohydrins, **17**, was detected. This observation suggests that the carboxylate is essential for the hydrolysis of the vinyl sulfide. Furthermore, there was no reaction of the alcohol, **18**, prepared from the LAH reduction of **11c**, under the iodolactonization conditions. In fact, mercuric ion catalyzed hydrolysis of the homoallylic alcohol, **18**, under conditions reported by Grieco[6g] failed to give the ketone or an iodo ether.



17a, X = OH; Y = I
17b, X = I; Y = OH

18

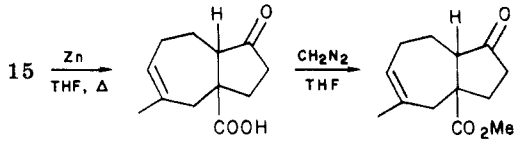


19

The failure to isolate **19** from the iodolactonization reaction of **11c** may indicate that the rate of hydrolysis of the vinyl sulfide is faster than the rate of iodolactonization.

A mechanism which accounts for these observations is shown in Scheme III. The vinyl sulfide hydrolysis may be viewed as a preferential iodolactonization of the vinyl sulfide, which leads eventually to the angular iodide **20**. The sequence of events at this point must be either nucleophilic deiodination followed by iodolactonization (path a) or iodolactonization followed by nucleophilic deiodination (path b), eventually leading to **15**.

Reductive elimination of iodine in **15** was accomplished with excess zinc in refluxing THF and afforded the keto acid **21**, which was immediately esterified with diazomethane to the ester **22** (mp 83–84.5 °C). The overall yield from **15** to **22** was 95%.

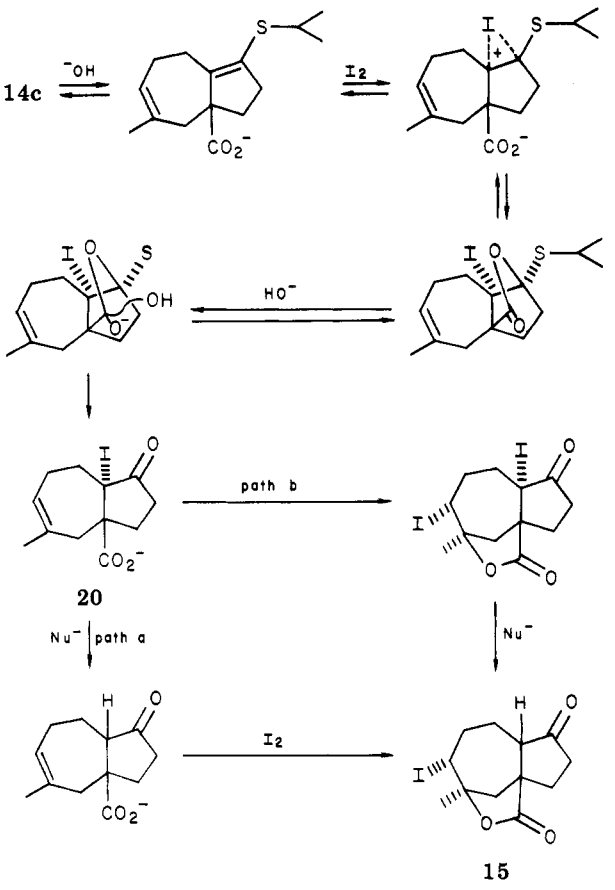


21 22

The efficient transformation of **11c** to **22**, albeit circuitous, involves four operations in an overll yield of 52% and represents the "formal hydrolysis" of the vinyl sulfide **11b** or **11c**. This sequence of events is noteworthy since all literature methods investigated failed to hydrolyze the vinyl sulfide directly.

(10) We have tentatively assigned the cis stereochemistry at the ring fusion primarily because of C-13 data and the expectation that the *cis*-lactone of **15** is thermodynamically more stable than trans. C-13 NMR spectra of **15** and **22** show clearly only one isomer. An attempt to equilibrate **22** in NaOMe/MeOH resulted in the 100% recovery of the isomer shown as *cis*-**22**.

Scheme III



Experimental Section

Melting points were determined on a Thomas-Hoover Unimelt apparatus and are uncorrected. Proton NMR spectra were recorded on Varian T-60A and JEOL MH 100 instruments and are reported relative to internal Me_4Si. Infrared spectra were taken on a Perkin-Elmer 457 grating spectrophotometer. Carbon-13 NMR were taken on a JEOL FX-90Q instrument. High-resolution mass spectra were taken on an AEI-902 spectrometer and regular mass spectra were taken on a Finnegan 4021 GC-MS instrument. Microanalyses were carried out by Spang Microanalytical Laboratory, Eagle Harbor, MI.

General Procedure for the Preparation of 3. To 31 mmol (4.35 mL) of diisopropylamine at 0 °C in 30 mL of dry THF was added 30 mmol (20 mL, 1.50 M) of *n*-BuLi in hexane. The resulting solution was stirred 15 min at 0 °C, cooled to −30 °C, and transferred to a slurry of 30 mmol of triphenylphosphonium fluoroborate in 90 mL of THF at −30 °C. The resulting clear red solution of the ylide was stirred for 30 min at −30 °C and transferred to 32 mmol of sulfenylating agent in 150 mL of THF. After 1 h at −30 °C, the reaction was quenched by the addition of 400 mL of water. The mixture was extracted three times with 250-mL portions of chloroform. The extracts were dried over anhydrous sodium sulfate, filtered through a Celite pad with the aid of suction, and concentrated to an oily solid. The crude product was taken up in hot chloroform and crystallized by the addition of ethyl acetate to yield 80–84% of analytically pure **3**.

3a: mp 201–202.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.4–7.9 (20 H, m), 1.4–2.1 (4 H, m); IR ($CDCl_3$) 3050, 1590, 1440, 1080 cm^{-1}. Anal. Calcd for $C_{27}H_{24}SPBF_4$: C, 65.08; H, 4.86; S, 6.21. Found: C, 65.02; H, 4.92; S, 6.35.

3b: mp 166–167 °C; ^{1}H NMR ($CDCl_3$) δ 7.73 (15 H, m), 1.3–2.0 (4 H, m), 1.73 (3 H, s); IR ($CDCl_3$) 3070, 1590, 1440, 1420, 1220, 1190, 1060 cm^{-1}. Anal. Calcd for $C_{22}H_{22}SPBF_4$: C, 60.57; H, 5.08; S, 7.35. Found: C, 60.55; H, 5.08; S, 7.51.

3c: mp 176–178 °C; ^{1}H NMR ($CDCl_3$) δ 7.60 (15 H, m), 2.55 (1 H, heptet, J = 7 Hz), 1.3–2.0 (4 H, m), 0.95 (6 H, d, J = 7 Hz); IR ($CDCl_3$) 2920, 2860, 1590, 1100 cm^{-1}. Anal. Calcd for $C_{24}H_{26}SPBF_4$: C, 62.08; H, 5.64; S, 6.91; P, 6.67. Found: C, 61.93; H, 5.61; S, 6.97; P, 6.59.

7: mp 185–197.5 °C (from chloroform–ethyl acetate); at 0 °C 50% **7** was formed; ^{1}H NMR ($CDCl_3$) δ 7.7–8.1 (15 H, m), 4.9–5.4 (1 H, m), 2.8–3.3 (2 H, m), 1.4–2.2 (8 H, m). Anal. Calcd for $C_{23}H_{26}S_2PBF_4$: C, 57.03; H, 5.41; S, 13.24. Found: C, 57.01; H, 5.23; S, 13.12.

9: mp 131–133 °C (from ethyl acetate); at 0 °C 10% **9** was isolated; ^{1}H NMR ($CDCl_3$) δ 7.4–7.9 (30 H, m), 4.3–4.8 (1 H, m), 3.2–1.4 (5 H, m), 1.20 (4 H, br t, J = 6 Hz), 0.50 (6 H, 2 overlapping d, J = 6, 6 Hz). anal. Calcd for $C_{45}H_{46}SP_2B_2F_8$: C, 63.25; H, 5.43; S, 3.75; P, 7.25. Found: C, 63.18; H, 5.53; S, 3.85; P, 7.31.

Vinyl Sulfide 11c. To 0.85 g (21 mmol) of potassium hydride (washed three times with ether) suspended in 50 mL of THF was added slowly 2.67 g (14.7 mmol) of **10** in 10 mL of THF. After 10 min at room temperature, 9.28 g (20 mmol) of **3c** was added in one portion to the clear yellow-orange solution of the enolate. The resulting slurry was heated to reflux for 3 days, after which the cooled reaction mixture was filtered through a Celite pad with the aid of suction and concentrated to ca. 7 g of a brown semisolid mass. The crude product was chromatographed on 150 g of silica and 3.22 g (78%) of **11c** was eluted with chloroform, as well as 0.11 g of a 1:1 mixture of **10** and **11c** and 0.36 g of recovered **10**. The yield of **11c** based on consumed **10** was 91%: ^{1}H NMR (CCl_4) δ 5.60 (1 H, br t), 3.60 (3 H, s), 2.4–1.9 (10 H, m), 1.73 (3 H, br s), 1.22 (3 H, d, J = 7 Hz); IR (CCl_4) 2900, 1735, 1400, 910 cm^{-1}; mass spectrum, m/e 280 (M^+), 237 (100%), 221, 179, 145, 91, 59. Anal. Calcd for $C_{16}H_{24}SO_2$: C, 68.53; H, 8.63; S, 11.43. Found: C, 68.28; H, 8.78; S, 11.40.

Vinyl Sulfide 11a. Compound **11a** was produced in 90% yield by the reaction of **3a** and **10** as was described in the previous experiment: ^{1}H NMR (CCl_4) δ 7.15 (5 H, br s), 5.65 (1 H, br t), 3.68 (3 H, s), 1.9–3.2 (10 H, m), 1.80 (3 H, br s); IR (CCl_4) 2950, 1735, 1480, 1440, 1200, 1165 cm^{-1}; mass spectrum, m/e 314 (M^+), 255 (100%), 205, 145. Anal. Calcd. for $C_{19}H_{22}SO_2$: C, 72.57; H, 7.05; S, 10.20. Found: C, 72.40; H, 7.20; S, 10.15.

Vinyl Sulfide 11b and Sulfide 13. Compound **11b** was produced in 50% yield by the reaction of **3b** and **10** as was described for the preparation of **11b**. Compound **13** was also produced in 50% yield. The two products were separated on a silica column with 3:1 petroleum ether–ether.

11b: ^{1}H NMR (CCl_4) δ 5.53 (1 H, br t), 3.58 (3 H, s), 2.18 (3 H, s), 1.8–2.8 (10 H, m), 1.72 (3 H, br s); IR (CCl_4) 2940, 1720, 1435, 1160 cm^{-1}; mass spectrum, m/e 252 (M^+), 237, 205, 193 (100%), 149, 145, 91, 57. Anal. Calcd for $C_{14}H_{20}SO_2$: C, 66.63; H, 7.99; S, 12.70. Found: C, 66.62; H, 7.93; S, 12.57.

13: ^{1}H NMR (CCl_4) δ 5.50 (1 H, br t), 3.65 (3 H, s), 2.2–2.8 (6 H, m), 2.03 (3 H, s), 1.80 (3 H, br s); IR (CCl_4) 2950, 1725, 1435 cm^{-1}; mass spectrum, m/e 228 (M^+), 196, 181 (100%), 180, 169, 93, 79.

Acid 14c. An aqueous solution of 10% NaOH (25 mL) and 1.41 g (5.0 mmol) of **11c** were refluxed for 20 h. The aqueous solution was washed once with 10 mL of ether, acidified with 10% HCl, and extracted with three 50-mL portions of chloroform. The combined extracts were dried over sodium sulfate, filtered through a pad of Celite with the aid of suction, and concentrated in vacuo to 1.33 g (99%) of **14c**, which crystallized upon standing. An analytical sample was prepared by recrystallization from a chloroform–ether mixture: mp 86–88 °C; ^{1}H NMR ($CDCl_3$) δ 11.0 (1 H, s), 5.62 (1 H, br t), 1.9–3.5 (10 H, m), 1.80 (3 H, br s), 1.22 (6 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) 182.4, 147.3, 136.5, 131.5, 126.8, 59.9, 41.9, 36.6, 35.4, 34.5, 26.7, 23.7 ppm; IR ($CDCl_3$) 3000–3300, 1700, 1446, 1310, 1140, 960 cm^{-1}. Anal. Calcd for $C_{15}H_{22}SO_2$: C, 67.63; H, 8.32; S, 12.04. Found: C, 67.49; H, 8.29; S, 12.14.

Acid 14a. Compound **14a** was prepared in 90% yield by the base hydrolysis of **11a** as was described in the previous experiment: mp 144–146 °C; ^{1}H NMR ($CDCl_3$) δ 11.0 (1 H, s), 7.25 (5 H, s), 5.68 (1 H, br t), 1.6–3.2 (10 H, m), 1.83 (3 H, br s); IR ($CDCl_3$) 3500, 2940, 1740, 1700, 1585, 1440, 1025 cm^{-1}; mass spectrum, m/e 300 (M^+), 255, 191 (100%), 145, 91, 77. Anal. Calcd for $C_{18}H_{20}SO_2$: C, 71.96; H, 6.71; S, 10.67. Found: C, 71.72; H, 6.60; S, 10.80.

Acid 14b. Compound **14b** was prepared in 97% yield by the reaction of NaOH with the ester **11b** as was described for the preparation of **14c**: mp 122–123 °C; ^{1}H NMR ($CDCl_3$) δ 11.2 (1 H, br s), 5.65 (1 H, br t), 1.4–3.0 (10 H, m), 2.23 (3 H, s), 1.75 (3 H, br s); IR ($CDCl_3$) 3150, 2935, 2860, 1700, 1440, 1310, 1120 cm^{-1}; mass spectrum, m/e 238 (M^+), 223, 193, 177, 145, 91. Anal. Calcd

for $C_{13}H_{18}SO_2$: C, 65.51; H, 7.61; S, 13.45. Found: C, 65.56; H, 7.52; S, 13.37.

Iodo Lactone 16. A 25-mL solution of saturated sodium bicarbonate was combined with a 2.5-mL solution of 102 mg of I_2 and 200 mg of KI. To this solution was added 60 mg (0.20 mmol) of acid **14a**, and the resulting mixture was stirred in the dark for 20 h. The crude reaction mixture was extracted three times with 10-mL portions of chloroform. The extracts were washed once with 10 mL of a 10% sodium bisulfite solution and dried over anhydrous magnesium sulfate. The dried solution was filtered through a pad of Celite with the aid of suction and concentrated to 92 mg of a brown solid. The crude product was triturated with a chloroform–ether mixture to afford 79 mg (93%) of material. An analytical sample was obtained by recrystallization from chloroform–ether: mp 152.5–154 °C; ^{1}H NMR ($CDCl_3$) δ 7.28 (5 H, s), 4.63 (1 H, br s), 1.8–3.2 (10 H, m), 1.73 (3 H, s); IR ($CDCl_3$) 2930, 1765, 1580, 1385, 1135, 965, 915 cm^{-1}; mass spectrum, m/e 426 (M^+), 299, 255 (100%), 145, 91, 77. Anal. Calcd for $C_{18}H_{19}SO_2I$: C, 50.71; H, 4.49; S, 7.52; I, 29.72. Found: C, 50.82; H, 4.51; S, 7.38; I, 29.77.

Keto Lactone 15. A solution comprised of 4.0 g of I_2 and 8.0 g of KI in 125 mL of water was added to a solution of 1.33 g (5.0 mmol) of acid **14c** in 100 mL of water. The reaction was stirred for 2 days at room temperature in the dark. The crude, dark reaction mixture was extracted three times with 50 mL chloroform. The extracts were washed once with 25 mL of 10% sodium bisulfite, dried over anhydrous sodium sulfate, and filtered through a Celite pad with the aid of suction. The crude material obtained by concentration of the dried chloroform extracts were chromatographed on 150 g of silica gel, using ether as the eluant, to yield 0.86 g (50%) of **15**, mp 167–169 °C. Compound **15** was also prepared from **14b** in 55% yield as described above: ^{1}H NMR ($CDCl_3$) δ 4.58 (1 H, br s), 1.60–3.10 (11 H, m), 1.75 (3 H, s); ^{13}C NMR ($CDCl_3$) 215.2, 180.2, 85.8, 56.2, 51.5, 40.8, 40.1, 36.1, 31.5, 30.5, 29.7, 22.5 ppm; IR ($CDCl_3$) 2975, 2940, 2860, 1765, 1740, 1225, 1150, 1130 cm^{-1}; mass spectrum, m/e (no M^+), 207, 179, 144, 130, 101, 91, 72 (100%); CI mass spectrum (CH_4), m/e 335 ($M^+ + 1$), 307, 207, 189, 171, 191, 129, 83, 41 (100%). Anal. Calcd for $C_{12}H_{15}IO_3$: C, 43.13; H, 4.53; I, 37.98. Found: C, 43.13; H, 4.50; I, 37.87.

Keto Ester 22. A solution of 0.65 g (2.0 mmol) of keto iodo lactone **15** in 50 mL of THF containing 0.50 g of zinc was refluxed for 3 h. The THF solution was filtered through a pad of Celite and concentrated to an oil which was partitioned between 25 mL each of chloroform and water. The chloroform layer was dried over anhydrous sodium sulfate, filtered through a Celite pad, and concentrated to an oil. The crude acid **21** so obtained was taken up in 50 mL of THF and was treated with 10 mL of diazomethane in ether (ca. 1 mmol/mL) at 0.5-h intervals three times. The reaction was stirred an additional 1 h after the third addition, filtered through a pad of Celite, and concentrated to 434 mg (100%) of an oil. The crude oil was chromatographed on 200 g of silica and was eluted with chloroform to yield 310 mg (90%) of **22**: mp 83–84.5 °C; ^{1}H NMR ($CDCl_3$) δ 5.42 (1 H, br t, J = 5 Hz), 3.63 (3 H, s), 3.07 (1 H, br t, J = 7 Hz), 2.62 (1 H, d of d, J = 15, 16 Hz), 2.25–2.45 (3 H, m), 1.95–2.15 (4 H, m), 1.85–1.95 (2 H, m), 1.70 (3 H, br s); ^{13}C NMR ($CDCl_3$) 217.8, 176.2, 134.1, 126.3, 55.1, 52.5, 52.0, 37.3, 35.4, 33.5, 26.5, 25.4, 23.5 ppm; IR ($CDCl_3$) 2925, 2850, 1740, 1732, 1210 cm^{-1}; mass spectrum, m/e 222 (M^+), 163, 141, 91, 82 (100%), 79, 68, 54. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.15; H, 8.14.

Vinyl Sulfide 8. Sodium hydride (150 mg after washing three times each with 15 mL of ether, 6.2 mmol) was suspended in 50 mL of THF and 2.91 g (6.0 mmol) of **7** was added in one portion. The reaction was refluxed for 1 h and cooled and 0.64 mL of (96.3 mmol) of benzaldehyde in 10 mL of THF was added. The reaction was refluxed for 1 day, cooled, filtered through a pad of Celite with the aid of suction, and concentrated to 3 g of an oily brown solid. The crude material was triturated with petroleum ether to obtain 1.38 g of crude oil which was chromatographed on 40 g of silca, eluting with petroleum ether–ether (5:1). There was obtained 0.80 g (59%) of vinyl sulfide **8**, as a mixture of isomers: ^{1}H NMR (CCl_4) δ 7.1–7.5 (5 H, m), 6.5 and 6.2 (1 H, br s), 2.7 (4 H, br s), 2.23, 2.07, 2.02, 1.92 (6 H, s); mass spectrum, m/e 224 (M^+), 209, 194, 177, 160, 129, 115 (100%), 105, 91, 77.

Hydroxy Vinyl Sulfide 18. A solution of 210 mg (0.75 mmol) of vinyl sulfide **14c** 4 mL of ether was slowly added to 58 mg (1.6 mmol) of lithium aluminum hydride suspended in 5 mL of ether. The reaction was stirred for 2 h at room temperature, cooled to 0 °C, and excess hydride was decomposed by the careful addition of saturated sodium sulfate until no gray solid was apparent. The ether solution was filtered through a pad of Celite with the aid of suction and concentrated to 157 mg (83%) of an oil: ^{1}H NMR ($CDCl_3$) δ 5.7 (1 H, br t), 3.50 (2 H, s), 2.7–3.5 (1 H, heptet), 1.6–2.7 (11 H, m), 1.73 (3 H, br s), 1.22 (6 H, d, J = 6.5 Hz); IR ($CDCl_3$) 3400, 2955, 2920, 2850, 1480, 1380, 1365, 1240, 1030, 925, 815 cm^{-1}; mass spectrum, m/e 252 (M^+), 221 (100%), 209, 179, 145, 91, 79, 77.

Registry No. 3a, 58992-26-0; **3b**, 76757-63-6; **3c**, 76757-65-8; **5**, 76757-83-0; **7**, 76757-67-0; **8**, 76757-68-1; **9**, 76757-70-5; **10**, 76757-71-6; **11a**, 76773-01-8; **11b**, 76757-72-7; **11c**, 76757-73-8; **13**, 76757-74-9; **14a**, 76757-75-0; **14b**, 76757-76-1; **14c**, 76757-77-2; **15**, 76757-78-3; **16**, 76757-79-4; **18**, 76757-80-7; **22**, 76757-81-8; diisopropylamine, 108-18-9; *N*-(phenylthio)succinimide, 14204-24-1; methyl disulfide, 624-92-0; isopropyl disulfide, 4253-89-8.

Preparation and Characterization of 1,8,19,26-Tetraoxa[8.8](2,6)naphthalenophane-3,5,21,23-tetrayne and Related Donut-Shaped Cyclophanes

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The synthesis of two representative members of the little explored class of large donut-shaped molecules is described. Investigation of their NMR spectra shows them to possess large cavities.

We report here the preparation, characterization, and some initial studies of the donut-shaped macrocyclophanes **6** and **7** (Figure 1). Macrocyclophanes[1,2] of this general type are of some interest as they may serve as the structural basis for constructing large but conformationally well-defined molecular frameworks.[3-6] This is particularly

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