Reactions of Perfluorocycloalkenones with Nucleophiles†

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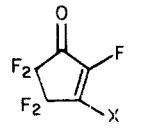
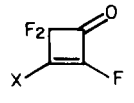
The reactions of perfluorocyclopent-2-en-1-one and perfluorocyclobutenone with various nucleophiles have been studied. The enones are attacked by nucleophiles at C-3 via an addition–elimination sequence to afford the 3-substituted perfluorinated enones. Multiple addition products were isolated when the enones were treated with mercaptans. Perfluorocyclopent-2-en-1-one reacted with potassium acetate to give, after hydrolysis, 3-hydroxy-2,4,4,5,5-pentafluorocyclopent-2-en-1-one. Hydrolysis of 1,2-dithiomethoxy-3,4,4-trifluorocyclobutenyl hexafluoroantimonate afforded 3,4-dithiomethoxycyclobutene-1,2-dione in low yield.

The chemistry of fluoro ketones is well established,[1] but α,β-unsaturated perfluorinated ketones have received little attention owing to their general unavailability. As part of a program concerned with the synthesis and chemistry of perfluorocycloalkenones,[2] we became interested in the reactions of perfluorocyclopent-2-en-1-one (1) and perfluorocyclobutenone (2) with various nucleophiles. In this paper we report the results of our study.

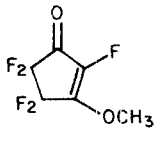
As anticipated, enones 1 and 2 are attacked by nucleophiles at C-3 via an addition–elimination sequence to afford the 3-substituted perfluorinated enones.[3] For example, 1 and 2 reacted with 2 equiv of aniline or tosylhydrazide to give 3, 4, or 5 in good yields as the only isolated products. Further treatment with excess amine for prolonged periods yielded no additional substitution products even under forcing conditions. The structural assignments are based upon the IR and ^{19}F NMR spectra of the products. Enone 3 showed a doublet at ϕ −117.8 (2 F, $J_{2,5}$ = 9 Hz) that was assigned to the fluorines on C-5, a doublet at ϕ −126.8 (2 F, $J_{2,4}$ = 7 Hz) assigned to the fluorines on C-4, and a multiplet at ϕ −147.4 for the remaining vinyl fluorine. The multiplet at ϕ −147.4 was assigned to F-2 by analogy with 6 and 7 in which the vinylic fluorines appear at −140.6 (m, J = 13.8, 5.4 Hz) and −108 ppm, respectively.[4,5] In addition, the vinylic fluorine of enone 18 (vide infra), the structure of which was determined by X-ray crystallographic analysis, appears at ϕ −145.3 as a multiplet. The doublets at ϕ −117.8 (F-5) and −126.8 (F-4) were also assigned by analogy with 7 in which they appear at ϕ −123 and −127, respectively. The chemical shifts and coupling constants of the other derivatives were assigned similarly.



1, X = F
3, X = NHC_6H_5
5, X = $NHNHSO_2C_7H_7$



2, X = F
4, X = NHC_6H_5



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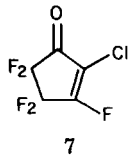

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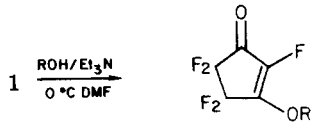
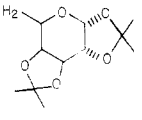
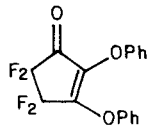
Enone 1 reacted readily with alcohols in the presence of 1 equiv of triethylamine at 0 °C. In this manner, methanol, phenol, *n*-decanol, and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose yielded enones 6 and 8–10 in good to moderate yields after chromatography.



6, R = CH_3
8, R = Ph
9, R = $(CH_2)_9CH_3$
10, R =



Allyl alcohol gave only complex mixtures. The structures of these derivatives were readily confirmed by their ^{19}F NMR spectra which were analogous to the amine spectra previously described. Interestingly, 6 and 8–10 are inert to water, in contrast to 1 and 2 which are readily hydrolyzed. The enones are also relatively inert to further substitution by alkoxides. For instance, enone 8 was completely inert to excess sodium phenolate at 25 °C for a period of 72 h. Refluxing this mixture for 24 h afforded only trace amounts of 11, 32% recovered 8, and material of high molecular weight. This behavior stands in contrast to 12 which affords 13 in 76% overall yield from perfluorocyclopentene.



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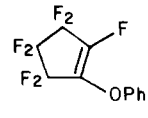

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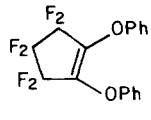
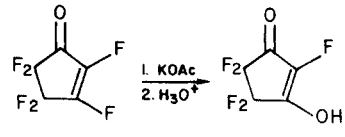


13

When 1 was treated with potassium acetate followed by hydrolysis with dilute acid, 14 was isolated in 50% yield



1 14

† Contribution No. 2791.

(1) Chambers, R. D. "Fluorine in Organic Chemistry"; Wiley: New York, 1973; p 216.
(2) (a) Smart, B. E.; Krespan, C. G. *J. Am. Chem. Soc.* **1977**, *99*, 1218. (b) Krespan, C. G.; Smart, B. E. U.S. Patent 4 021 489, 1977.
(3) Scherer, O.; Horlein, G.; Millener, H. *Chem. Ber.* **1976**, *99*, 1966.
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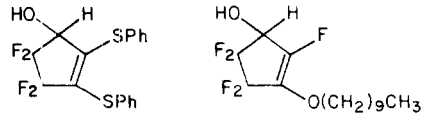
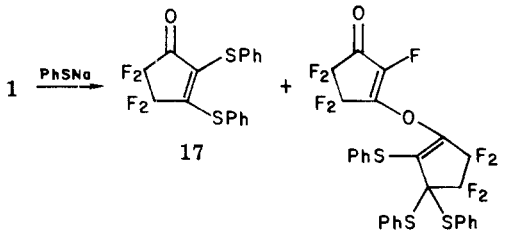
after chromatography and distillation. Enol **14** was obtained as a low-melting, hygroscopic semisolid that was acidic to litmus. This material is consistent with descriptions given it in previous reports.[6] The structure of **14** follows from its ^{1}H NMR [δ 11.48 (s)] and ^{19}F NMR [ϕ −124.6 (d, 4 F, J = Hz), −155.8 (quintet, 1 F, J = 8 Hz)] which support the enol form. Presumably the equivalence of the CF_2 groups in the ^{19}F NMR is the result of rapid proton exchange rather than accidental coincidence.

Only complex mixtures were obtained when **1** was treated with sodium borohydride, but enones **17** and **9** gave **15** and **16** in 75% and 98% yields, respectively.



15 **16**

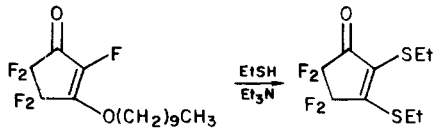
One equivalent of sodium thiophenoxide reacted rapidly with **1** at 25 °C to give a 30% yield of **17** and a 27% yield of **18**. The structure of the bright yellow enone **17** was



17 **18**

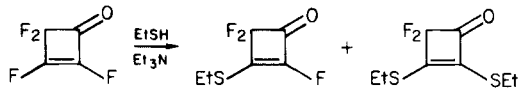
readily confirmed by IR, ^{19}F NMR, and mass spectral analyses, but the structure of **18** was assigned by X-ray crystallography.[7] Enone **17** must result from the reaction of 3-thiophenoxy-2,4,4,5,5-pentafluorocyclopent-2-en-1-one (**19**) with thiophenoxide, but all efforts to detect **19** were unsuccessful. The formation of **18** is most easily explained by reaction of **17** with thiophenoxide to produce the enolate anion which subsequently reacts with **1**. The ability of sulfur to stabilize an adjacent negative charge underlies the fact that thiophenoxide reacts more rapidly with **17** and **19** than with **1**.

When **1** was treated with 2 equiv of thiophenoxide at −30 °C, enone **17** was isolated in 68% yield, and only traces of **18** were detected. The low yield of **18** is consistent with the fact that treatment of **18** with 1 equiv of thiophenoxide gave **17** in 89% yield as the only detectable product. In a similar experiment, treatment of enone **9** with ethanethiol afforded **20** as the only reaction product.



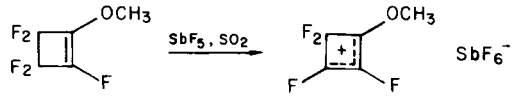
9 **20**

In contrast to **1**, enone **2** afforded both mono- and disubstituted sulfide derivatives. Perfluorocyclobutenone readily reacted with 1 equiv of ethanethiol in the presence of triethylamine to give **21** and **22** in 6% and 20% yields, respectively. The low yields associated with the synthesis of **2**, **21**, and **22** prompted us to explore an alternative route to these molecules.



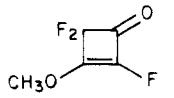
2 **21** **22**

Treatment of **23** with SbF_5 in SO_2 at −78 to −10 °C gave **24** which was isolated as a colorless crystalline salt.[8]



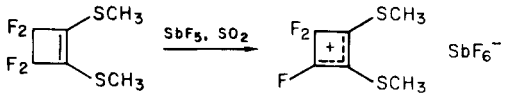
23 **24**

Hydrolysis of this salt gave cyclobutenone **25** in 47% yield.[8]



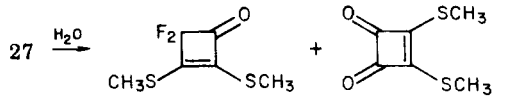
25

When olefin **26**[9] was reacted with SbF_5 in SO_2 at −78 to −10 °C, cation **27** was isolated in 67% yield as a deep blue



26 **27**

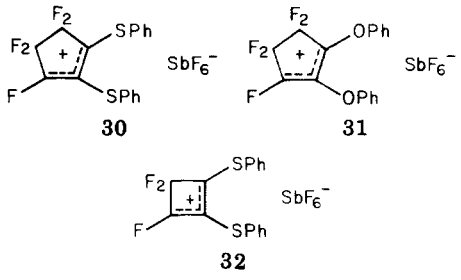
crystalline solid. The structure of **27** was deduced from its ^{19}F NMR spectrum (SO_2, −45 °C, external reference) which consisted of a triplet at ϕ −53.7 (1 F, J = 10 Hz) and a doublet at ϕ −92.9 (2 F, J = 10 Hz). When hydrolyzed, **27** unfortunately gave **28** and **29** in only 10% and 7%



29 **28**

isolated yields, respectively. Dione **29** is briefly mentioned in the literature (mp 130 °C), but no accompanying physical or spectral data were reported.[10] We obtained **29** as a yellow solid (mp 135.5–137 °C) which exhibited two carbonyl absorptions in the infrared (1745 and 1725 cm^{-1}) and a singlet (δ 2.92) for its ^{1}H NMR spectrum.

Other cation salts (**30–32**) were prepared and hydrolyzed, but only complex mixtures of products were obtained.



30 **31** **32**

Experimental Section

General Methods. Melting points were determined with a Hoover capillary melting point apparatus and are uncorrected. Boiling points are also uncorrected. Infrared spectra were determined on a Perkin-Elmer 137 spectrometer. ^{1}H NMR spectra were obtained in chloroform-*d* on a Varian A-60 or EM-390 spectrometer and are referenced to internal tetramethylsilane. The ^{19}F NMR spectra were obtained on a Varian XL-100 spec-

(6) (a) Stockel, R. F.; Beachem, M. T.; Megson, F. H. *J. Org. Chem.* **1965**, *30*, 1629. (b) Bekker, R. A.; Popkova, V. Y.; Knunyants, I. L. *Bull. Acad. Sci. USSR, Div. Chem. (Engl. Transl.)* **1978**, *27*, 430.

(7) Harlow, R. L.; Card, P. J., unpublished results.

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trometer and are referenced to internal trichlorofluoromethane.

UV spectra were determined on a Cary 17 spectrophotometer. High-pressure liquid chromatography was performed on a Waters Prep LC/System 500 instrument. All reactions were performed under a nitrogen atmosphere.

3-(Phenylamino)pentafluorocyclopent-2-en-1-one (3). A solution of 5.7 g (30 mmol) of perfluorocyclopent-2-en-1-one (1)[2] in 100 mL of chloroform at −30 °C was treated dropwise with 5.56 g (60 mmol) of freshly distilled aniline. The mixture was stirred at 0 °C for 45 min and then at room temperature for 1 h. Removal of the solvent under reduced pressure afforded a yellow solid. Chromatography on 100 g of silica gel with 3:1 hexane–ether gave 7.18 g (91%) of **3** as colorless crystals: mp 130–131 °C (hexane–chloroform); IR (KBr) 3230 (NH), 1735 (C=O), 1620 (C=C) cm^{-1}; ^1H NMR δ 7.35 (m, aromatic); ^{19}F NMR ϕ −117.8 (d, 2 F, J = 9 Hz), −126.8 (d, 2 F, J = 7 Hz), −147.4 (m, 1 F); UV (isooctane) λ_{max} 292 nm (ϵ 200 000), 219 (7120).

Anal. Calcd for $C_{11}H_6F_5NO$: C, 50.20; H, 2.30; N, 5.32. Found: C, 49.83; H, 2.31; N, 5.12.

3-(Phenylamino)-2,4,4-trifluorocyclobut-2-en-1-one (4). Reaction of enone **2**[2] with aniline as described above afforded **4** in 57% yield: mp 168–170 °C; IR (KBr) 3220 (NH), 1800 (C=O), 1650 (C=C) cm^{-1}; exact mass calcd for $C_{10}H_6F_3NO$ 213.0401, found 213.0408.

Anal. Calcd for $C_{10}H_6F_3NO$: C, 56.35; H, 2.84; N, 6.57. Found: C, 56.24; H, 2.97; N, 6.47.

2-(2,4,4,5,5-Pentafluoro-3-oxo-1-cyclopenten-1-yl)-*p*-toluenesulfonylhydrazide (5). Treatment of enone **1** as above with *p*-toluenesulfonylhydrazide gave **5** (97%): mp 172.5–173.5 °C (10:1 hexane–EtOAc); IR (KBr) 1760 (C=O), 1670 (C=C) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.45 (s, 3 H), 7.63 (q, 4 H, J = 8 Hz), 8.71 (br m, 1 H, NH), 10.7 (br m, 1 H, NH); ^{19}F NMR ϕ −116.1 (br m, 2 F), −125 (br m, 2 F), −153.6 (br m, 1 F); mass spectrum, m/e 356; UV (CH_3CN) λ_{max} 227 nm (ϵ 12 500), 279 (30 100).

Anal. Calcd for $C_{12}H_9F_5N_2O_3S$: C, 40.46; H, 2.55; N, 7.86; F, 26.66. Found: C, 39.84; H, 2.61; N, 8.10; F, 26.43.

3-Phenoxypentafluorocyclopent-2-en-1-one (8). A solution of 2.85 g (15 mmol) of **1** in 30 mL of glyme at −30 °C was treated dropwise with a solution of 1.51 g (15 mmol) of triethylamine and 1.41 g (15 mmol) of phenol in 10 mL of glyme. After complete addition, the mixture was stirred at room temperature for 1 h. Removal of the solvent under reduced pressure, chromatography (LC) of the residue with 6:1 hexane–ether, and Kugelrohr distillation afforded 2.25 g (57%) of **8**: bp 105–108 °C (1.5 mm); IR (neat) 1780 (C=O), 1670 (C=C) cm^{-1}; ^1H NMR δ 7.35 (m, aromatic); ^{19}F NMR ϕ −120.5 (d, 2 F, J = 9 Hz), −127.2 (d, 2 F, J = 6 Hz), −144.98 (tt, 1 F); mass spectrum, m/e 264; UV (isooctane) λ_{max} 227 nm (ϵ 10 800), 244 (14 000).

Anal. Calcd for $C_{11}H_5F_5O_2$: C, 50.02; H, 1.91. Found: C, 50.23; H, 1.93.

3-Methoxypentafluorocyclopent-2-en-1-one (6). Treatment of **1** with methanol as described above gave **6** in 30% yield: bp 40–45 °C (0.8 mm); IR (neat) 1757 (C=O), 1665 (C=C) cm^{-1}; ^1H NMR δ 4.36 (d, J = 4 Hz); ^{19}F NMR ϕ −120.8 (d, 2 F, J = 10 Hz), −127.4 (d, 2 F, J = 5.9 Hz), −155.6 (m, 1 F).[2,4]

3-(Decyloxy)pentafluorocyclopent-2-en-1-one (9). Reaction of **1** with *n*-decanol as described above gave **9** (33%) as a colorless liquid: bp (Kugelrohr) ~90 °C (0.15 mm); IR (neat) 1765 (C=O), 1660 (C=C) cm^{-1}; ^1H NMR δ 0.65–2.0 (m, 19 H), 4.6 (m, 2 H); ^{19}F NMR ϕ −120.95 (d, 2 F, J = 10 Hz), −127.3 (d, 2 F, J = 6 Hz), −154.9 (m, 1 F).

Anal. Calcd for $C_{15}H_{21}F_5O_2$: C, 54.87; H, 6.45. Found: C, 55.23; H, 6.45.

3-(1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose)-pentafluorocyclopent-2-en-1-one (10). Reaction of **1** with 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose as described above and chromatography on silica gel with 2:1 hexane–ether gave **10** (45%): bp (Kugelrohr) 135–140 °C (0.005 mm); IR (neat) 1760 (C=O), 1660 (C=C) cm^{-1}; ^1H NMR δ 1.4 (m, 12 H), 3.46 (m, 1 H), 4.28 (m, 3 H), 4.68 (m, 2 H), 5.51 (m, 1 H); ^{19}F NMR ϕ −120.7 (d, 2 F, J = 9 Hz), −127.3 (d, 2 F, J = 6 Hz), −152.3 (m, 1 F); mass spectrum, m/e 430.

Anal. Calcd for $C_{17}H_{19}F_5O_7$: C, 47.45; H, 4.45. Found: C, 47.77; H, 4.53.

1,2-Diphenoxyhexafluorocyclopentene (13). To a stirred solution of 4.24 g (20 mmol) of perfluorocyclopentene in 40 mL of glyme at −40 °C was added 4.64 g (40 mmol) of sodium phenoxide. After being stirred 2 h at room temperature, the mixture was quenched with water and extracted with petroleum ether. Drying ($MgSO_4$), concentration under reduced pressure, and Kugelrohr distillation afforded 5.48 g (76%) of **13** as a colorless oil: bp 138–142 °C (1.2 mm); IR (neat) 1680 (C=C), 1595 (C=C) cm^{-1}; ^1H NMR δ 6.65 (m, 2 H, ortho), 7.03 (m, 3 H); ^{19}F NMR ϕ −115.3 (m, 4 F), −130.8 (m, 2 F); mass spectrum, m/e 360.

Anal. Calcd for $C_{17}H_{10}F_6O_2$: C, 56.68; H, 2.80. Found: C, 56.55; H, 2.83.

3-Hydroxy-2,4,4,5,5-pentafluorocyclopent-2-en-1-one (14). To a stirred solution of 3.8 g (20 mmol) of **1** in 50 mL of glyme at −30 °C was added 2.0 g (20.5 mmol) of potassium acetate. After being stirred at −30 °C for 40 min and then at room temperature for 18 h, the mixture was poured into 5% HCl and extracted with ether. The organic layer was dried ($MgSO_4$) and concentrated to a brown residue that was chromatographed on silica gel with ether. Kugelrohr distillation afforded 1.97 g (49%) of **14** as a colorless semisolid: bp 110–115 °C (1 mm); ^1H NMR δ 11.48 (s); ^{19}F NMR ϕ −124.6 (d, 4 F, J = 8 Hz), −155.8 (quintet, 1 F, J = 8 Hz); exact mass calcd for $C_5HF_5O_2$ 187.9897, found 187.9876.

2,3-Dithiophenoxy-4,4,5,5-tetrafluorocyclopent-2-en-1-ol (15). A solution of 0.37 g (1 mmol) of **17** in 20 mL of methanol at 0 °C was treated with 0.021 g (0.57 mmol) of $NaBH_4$. After 30 min at 0 °C, the mixture was quenched by slow addition of water. Extraction with methylene chloride, drying ($MgSO_4$), and removal of the solvent under reduced pressure gave 0.280 g (75%) of **15** as a colorless solid: mp 99–101.5 °C; IR (KBr) 3540 (OH); ^1H NMR δ 2.02 (m, 1 H), 4.41 (br, 1 H), 7.46 (m, 10 H); ^{19}F NMR (decoupled) ϕ −102.5 (dd, J = 253 Hz, 11.5 Hz), −114.03 (ddd, J = 254, 11.5, 3 Hz), −121.04 (dd, J = 240, 11 Hz), −131.28 (ddd, J = 240, 11, 3 Hz); mass spectrum, m/e 372.

Anal. Calcd for $C_{17}H_{12}F_4OS_2$: C, 54.83; H, 3.25. Found: C, 54.88; H, 3.51.

3-(Decyloxy)-2,4,4,5,5-pentafluorocyclopent-2-en-1-ol (16). Reaction of **9** with $NaBH_4$ as described above afforded **16** in 98% yield as a colorless oil: IR (neat) 3400 (OH), 1740 (CF=C) cm^{-1}; ^1H NMR δ 0.88 (m, 3 H), 1.3 (m, 16 H), 3.38 (br, 1 H), 4.23 (m, 2 H), 4.73 (m, 1 H); ^{19}F NMR ϕ −114.7 (q, 2 F, J = 246 Hz), −124.6 (q, 2 F, J = 242 Hz), −147.4 (m, 1 F).

Reaction of 1 with 2 Equiv of Sodium Thiophenoxide. Preparation of 17. To a stirred solution of 8.55 g (45 mmol) of **1** in 100 mL of glyme at −30 °C was added 13.1 g (100 mmol) of sodium thiophenoxide. After the mixture was stirred overnight at room temperature and the solvent removed under reduced pressure, chromatography on silica gel with 3:1 hexane–ether gave 11.28 g (68%) of **17** as a bright yellow crystalline solid: mp 36.5–38 °C (hexane–ether); IR (KBr) 1760 (C=O), 1580 (C=C) cm^{-1}; ^1H NMR δ 7.2–7.7 (aromatic); ^{19}F ϕ −109.4 (t, 2 F, J = 3.3 Hz), −126.3 (t, 2 F, J = 3.3 Hz); mass spectrum, m/e 370; UV (isooctane) λ_{max} 244 nm (ϵ 11 300), 327 (10 700).

Anal. Calcd for $C_{17}H_{10}F_4OS_2$: C, 55.13; H, 2.72; S, 17.31; F, 20.51. Found: C, 55.49; H, 2.78; S, 17.71; F, 20.33.

Reaction of 1 with 1 Equiv of Sodium Thiophenoxide. Isolation of 18. Treatment of 2.85 g (15 mmol) of **1** with 1.98 g (15 mmol) of sodium thiophenoxide at 25 °C as described above afforded an oily yellow residue. Chromatography (LC) with 6:1 hexane–ether gave two main fractions.

Fraction I, 17, 650 mg (30%).

Fraction II, 18: 690 mg (31%); colorless solid; mp 124.5–125.5 °C (hexane–ether); IR (Nujol) 1760 (C=O), 1675 (C=C), 1620 (C=C) cm^{-1}; ^1H NMR δ 7.41 (m, aromatic), 7.83 (m, aromatic); ^{19}F ϕ −108.6 (unresolved dd, 2 F, J = 6, 6 Hz), −114.6 (q, 2 F, J = 6, 6, 6 Hz), −120.4 (d, 2 F, J = 9 Hz), −126.9 (d, 2 F, J = 6 Hz), −145.3 (m, 1 F); UV (isooctane) λ_{max} 218 nm (ϵ 23 100).

Anal. Calcd for $C_{28}H_{15}F_9O_2S_3$: C, 51.69; H, 2.32. Found: C, 52.03; H, 2.40.

2,3-Dithioethoxy-4,4,5,5-tetrafluorocyclopent-2-en-1-one (20). A solution of 5.7 g (30 mmol) of **1** in 30 mL of glyme at −30 °C was treated dropwise with a solution of 3.72 g (60 mmol) of ethanethiol and 6.06 g (60 mmol) of triethylamine in 30 mL of glyme. After the mixture was stirred 18 h at room temperature, the solvent was removed under reduced pressure. Chromatography on silica gel with 6:1 hexane–ether and Kugelrohr distillation afforded 3.37 g (41%) of **20** as a light yellow oil: bp 110–120 °C (0.1 mm); IR (neat) 1740 (C=O), 1680 (C=C) cm^{-1}; ^1H NMR δ

1.31 (t, 3 H, J = 7.5 Hz), 1.45 (t, 3 H, J = 7.5 Hz), 3.35 (q, 2 H, J = 7.5 Hz), 3.39 (q, 3 H, J = 7.5 Hz); ^{19}F NMR ϕ -108.7 (t, 2 F, J = 1.5 Hz), -125.2 (t, 2 F, J = 1.5 Hz); mass spectrum, m/e 274.

Anal. Calcd for $C_9H_{10}F_4OS_2$: C, 39.41; H, 3.67. Found: C, 39.47; H, 3.62.

Reaction of 9 with Ethanethiol. Treatment of **9** with 1 equiv of ethanethiol and triethylamine as described above afforded an inseparable mixture of **9** and **20** in a 3:7 ratio.

3-Thioethoxy-2,4,4-trifluorocyclobutenone (21) and 2,3-Dithioethoxy-4,4-difluorocyclobutenone (22). Treatment of 1.59 g (11.35 mmol) of **2** with 0.7 g (11.35 mmol) of ethanethiol and 1.41 g (14 mmol) of triethylamine as described above gave a brown residue which was separated into two fractions by preparative thin-layer chromatography with 9:1 hexane-ether.

Fraction I, 22: 470 mg (20%); IR (neat) 1750 (C=O), 1735 (C=C) cm^{-1}; ^{1}H NMR δ 1.40 (t, 3 H, J = 8 Hz), 1.46 (t, 3 H, J = 7 Hz), 3.25 (q, 2 H, J = 8 Hz), 3.27 (q, 2 H, J = 7 Hz); ^{19}F NMR ϕ -102.65 (s); mass spectrum m/e 224; UV (isooctane) λ_{max} 215 nm (ϵ 6940), 230 (7970), 300 (15 500).

Anal. Calcd for $C_8H_{10}F_2OS_2$: C, 42.84; H, 4.49. Found: C, 43.15; H, 4.45.

Fraction II, 21: 130 mg (6.3%); IR (neat) 1820 (C=O), 1640 (C=C) cm^{-1}; ^{1}H NMR δ 1.48 (t, 3 H, J = 8 Hz), 3.25 (q, 2 H, J = 8 Hz); ^{19}F NMR ϕ -107.3 (A of AB_2, J = 23 Hz), -110.12 (B of AB_2, J = 23 Hz); mass spectrum, m/e 182; UV (isooctane) λ_{max} 221 nm (ϵ 1700), 270 (23 200), 310 (851).

Anal. Calcd for $C_6H_5F_3OS$: C, 39.56; H, 2.77. Found: C, 39.77; H, 2.84.

1,2-Dithiomethoxy-3,4,4-trifluorocyclobutenyl Hexafluoroantimonate (27). Under anhydrous conditions, 4.92 g (22.6 mmol) of **26** was added dropwise to a solution of 4.88 g (22.6 mol) of SbF_5 in 25 mL of sulfur dioxide at -65 °C. The resulting homogeneous, deep blue solution was warmed to room temperature, while the sulfur dioxide was removed in a slow stream of nitrogen. The hexafluoroantimonate salt **27** was deposited as a deep blue crystalline solid in 67% isolated yield.

Hydrolysis of 27. 2,3-Dithiomethoxy-4,4-difluorocyclobutenone (28) and 3,4-Dithiomethoxycyclobutene-1,2-dione (29). The hexafluoroantimonate salt **27** (6.55 g, 15 mmol) was added cautiously in portions to vigorously stirred ice-water. After dissolution of the salt, the mixture was extracted with ether. The organic layer was dried ($MgSO_4$) and concentrated to a yellow mass that was separated into two components by thin-layer chromatography with 5:1 hexane-ether.

Fraction I, 28: 470 mg (10%); yellow solid; mp 33.5-35.5 °C (petroleum ether); IR (KBr) 1760 (C=O) cm^{-1}; ^{1}H NMR (benzene) δ 1.92 (s, 3 H), 2.12 (s, 3 H); ^{19}F NMR ϕ -102 (s); mass spectrum, m/e 196; UV (isooctane) 229 nm (ϵ 9337), 299 (16 375).

Anal. Calcd for $C_6H_6F_2OS_2$: C, 36.72; H, 3.08. Found: C, 36.70; H, 3.06.

Fraction II, 29: 280 mg (7%); yellow solid; mp 135.5-137 °C (ether-ethyl acetate); IR (KBr) 1745 (C=O), 1725 (C=O) cm^{-1}; ^{1}H NMR δ 2.92 (s); mass spectrum, m/e 174.

Anal. Calcd for $C_6H_6O_2S_2$: C, 41.36; H, 3.47. Found: C, 41.50; H, 3.51.

Registry No. 1, 24807-10-1; **2**, 60838-92-8; **3**, 74835-63-5; **4**, 74843-74-6; **5**, 74835-64-6; **6**, 60407-11-6; **8**, 74835-65-7; **9**, 74835-66-8; **10**, 74835-67-9; **13**, 74835-68-0; **14**, 66463-35-2; **15**, 74835-69-1; **16**, 74835-70-4; **17**, 74835-71-5; **18**, 74835-72-6; **20**, 74835-73-7; **21**, 74835-74-8; **22**, 74835-75-9; **26**, 13888-99-8; **27**, 74877-68-2; **28**, 74835-76-0; **29**, 54131-97-4; aniline, 62-53-3; *p*-toluenesulfonylhydrazide, 1576-35-8; phenol, 108-95-2; *n*-decanol, 112-30-1; 1,2:3,4-di-*O*-isopropylidene-D-galactopyranose, 4064-06-6; PhONa, 139-02-6; perfluorocyclopentene, 559-40-0; KOAc, 127-08-2; PhSNa, 930-69-8; EtSH, 75-08-1.

Microbial Stereodifferentiating Reduction of Carbonyl Compounds; Proposed Quadrant Rule[1]

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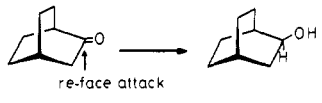
The stereochemistry of the isomeric alcohols obtained from microbial reduction (*Curvularia lunata* and *Rhodotorula rubra*) of the racemic modification of bicyclic (**5**, **8**, **23**), benzobicyclic (**11**, **14**, **17**), and tricyclic (**20**) ketones with a wide variation in molecular framework has led to the formulation of a quadrant rule which provides information on the absolute configuration of the substrate ketone.

Our continuing interest in the syntheses and chiroptical properties of various gyrochiral[2] cage-shaped molecules has led us to examine the stereochemistry of microbial reduction of tri- and pentacyclic cage-shaped C_2 ketones[3] (e.g., 9-*twist*-brendanone (**1**)) as well as that of the atropisomeric C_2 biphenyl-bridged ketone (**2**).[4]

Scheme I



3 (+)-(2S)-4

Illustrated in Figure 1 are the enantiomers **1** and **2**, which were found to be preferentially reduced by *Curvularia lunata* and *Rhodotorula rubra*, and they can be schematically represented by a *P*-C_2 ketone,[5] a quadrant projection formula obtained by looking from the oxygen side along the carbonyl axis (Figure 2).

Our formulation of the "C_2-ketone rule"[4b] stating that the microbes selectively reduce the *P*-C_2 ketones over the enantiomeric *M*-C_2 ketones[5] supplements the "Prelog

(1) Presented at the 26th IUPAC Congress, Sept 8, 1977, Tokyo, Japan, Abstracts p 63. For preliminary account of this work, see: Nakazaki, M.; Chikamatsu, H.; Naemura, K.; Hirose, Y.; Shimizu, T.; Asao, M. *J. Chem. Soc., Chem. Commun.* **1978**, 668-670. For review summarizing our studies on stereodifferentiating microbial reduction, see: Nakazaki, M.; Chikamatsu, H. *Kagaku no Ryoiki* **1977**, *31*, 819-833.

(2) This name is proposed to describe the symmetry of a shape which is chiral but not asymmetric. Cf.: Nakazaki, M.; Naemura, K.; Yoshihara, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3278-3284.

(3) In this paper, ketones are conveniently classified according to their symmetry: C_s ketones belong to the C_s point group and have the plane of symmetry coincident with the carbonyl plane; C_2 ketones belong to the C_2 point group and have the C_2 axis coincident with the carbonyl axis; C_1 ketones have no symmetry element passing through the carbonyl axis.

(4) (a) Nakazaki, M.; Chikamatsu, H.; Naemura, K.; Nishino, M.; Murakami, H.; Asao, M. *J. Chem. Soc., Chem. Commun.* **1978**, 667-668. (b) Nakazaki, M.; Chikamatsu, H.; Naemura, K.; Nishino, M.; Murakami, H.; Asao, M. *J. Org. Chem.* **1979**, *44*, 4588-4593.

(5) An inspection of the quadrant projection formula (Figure 1) should support the adequacy of our adopting *M* and *P* helicity[6] to describe these chiralities.

(6) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385-415.

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