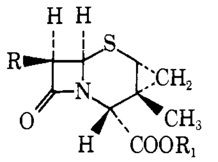
Table I. Spectral Data of 2,3-Methylenecephams[a]

Compound[c]	Solvent	3-CH_3	2-H[e]	4-H	6-H[d]	7-H[d]	Ir(cm^{-1})[b]
6	TFA	79	173 (6, 9.5)	310	320 (4.2)	361 (4.2)	1782
7	$CDCl_3$	95	165 (6.5, 8.5)	288	268 (4.0)	362 (4.0)	1785
8	TFA	101	174 (6, 9)	323	303 (3.8)	367 (3.8)	1785
9	$CDCl_3$	94	111 (5.5, 9.5)	304	305.5 (4.0)	338.5 (4.0)	1788
10	$CDCl_3$	88	114 (5.5, 8.0)	294	317 (4.0)	330 (4.0)	1788
11	$CDCl_3$	94	112 (6.0, 7.5)	298	301 (4.0)	338 (4.0)	1785
12	$CDCl_3$	85	114 (5.5, 8.0)	291	318 (4.0)	333 (4.0)	1790
16	$CDCl_3$	81	109 (5.0, 8.0)	277	290 (4.0)	335[e] (4.0, 8.5)	1780
17	$CDCl_3$	69	110 (5.5, 7.5)	303 (4.0)		321[e] (4.0, 8.0)	1787

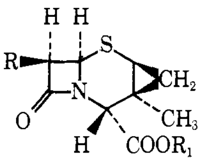
[a] NMR chemical shifts measured in Hz from TMS on a Varian HA-60 instrument, J (Hz) in parentheses. [b] Azetidinone C=O. [c] Satisfactory analyses were obtained for all new compounds. [d] Doublet. [e] Quartet.

possibly three, competing reactions of **2**. First is the reaction of **2** with HCl to give the chloromethylsulfoxide **5**, the major reaction product. Products **6**, **7**, and **8** arise from the diazosulfoxide intermediate by one or both of two possible routes; that is, via the sulfoxo carbene intermediate **3** or the pyrazoline **4**.

Inasmuch as our ultimate goal was to prepare tricyclic azetidinones for biological testing, the sulfoxides were reduced to the corresponding sulfides, and subsequently, the carboxyl protective group was removed. Thus, **6** and **8** were reduced with 1 equiv of phosphorus tribromide in dimethylformamide to the corresponding 2α,3α-methylenecepham (**9**) (22°, 20 min, 90%). Likewise, compound **7** was reduced to provide the corresponding 2β,3β-methylene (**10**) (94%).



9, R = Ft, R_1 = pNB;
11, R = Ft, R_1 = H;
15, R = NH_2, R_1 = H;
17, R = $PhCH_2CONH$, R_1 = H

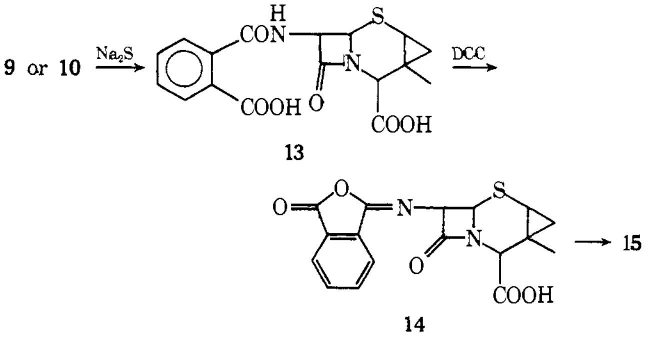


10, R = Ft, R_1 = pNB;
12, R = Ft, R_1 = H;
15, R = NH_2, R_1 = H;
16, R = $PhCH_2CONH$, R_1 = H

The p-nitrobenzyl group was removed by catalytic hydrogenation (Pd/C, THF-ethanol) from compounds **9** and **10** to give acids **11** and **12**. Compounds **11** and **12** exhibited no antibacterial activity as determined by a standard disk assay test.

Removal of the phthaloyl group was accomplished in accordance with the general procedures discussed earlier.[8] Scheme I illustrates the three-step sequence for conversion of **9** and **10** to their respective isomeric amino acids (**15**).

Scheme I



Hydrolysis of the phthalimido protected tricyclic cepham ester (2 equiv of $Na_2S{\cdot}9H_2O$, aqueous THF, 0°) gives the diacid **13** (>95%).[9] Treatment of **13** with 1 equiv of dicyclohexylcarbodiimide (THF, 25°) provides the phthalisoimido derivative **14** which is treated with 2 equiv of methylhydrazine (THF, −70°) to give the water soluble amino acid **15**. Both isomers (α- and β-methylene) of **15** were prepared by this route from their respective p-nitrobenzyl esters.

A Schotten-Baumann acylation of the isomers of **15** with phenylacetyl chloride gives the desired phenylacetamido compounds **16** and **17** (>50% yield) based on the diacid **13**. In a standard disk assay test both **16** and **17** at 2 mg/ml exhibited activity against: *Staphylococcus aureus, Bacillus subtilis, Sarcina lutea, Proteus vulgari,* and *Escherichi coli.* Of the two compounds, **16** consistently showed slightly better activity.

References and Notes

(1) D. O. Spry, *J. Chem. Soc., Chem. Commun.*, 671 (1973); G. Lowe and M. V. J. Ramsay, *J. Chem. Soc.*, 479 (1973); B. T. Golding and D. R. Hall, *ibid.*, 293 (1973); R. J. Stoodley, *Prog. Org. Chem.*, **8**, 102 (1973); S. Kukolja, *J. Am. Chem. Soc.*, **94**, 7590 (1972); J. C. Sheehan and M. Dadic, *J. Heterocycl. Chem.*, **5**, 779 (1968); S. Wolfe, J. B. Ducep, G. Kannengiesser, and W. S. Lee, *Can. J. Chem.*, **50**, 2907 (1972); R. Scartazzini, J. Gosteli, H. Bickel, and R. B. Woodward, *Helv. Chim. Acta*, **55**, 2567 (1972).

(2) S. Kukolja and S. R. Lammert, *Angew. Chem., Int. Ed. Engl.*, **12**, 67 (1973).

(3) G. Stork and J. Ficini, *J. Am. Chem. Soc.*, **83**, 4678 (1961).

(4) The reaction of sulfinyl chlorides and diazomethane has been reported. See, e.g., C. G. Venier, H.-H. Hsieh, and H. J. Barager, *J. Org. Chem.*, **38**, 17 (1973), and references therein. Note further the reaction of aromatic sulfines with diazo compounds in C. B. Venier and C. G. Gibbs, *Tetrahedron Lett.*, 2293 (1972).

(5) The chiral sulfur diastereomer of the chloromethylsulfoxide **5** was also a reaction product and was present in the mother liquor from which the major diastereomer crystallized. No attempt was made, however, to isolate this minor component.

(6) R. D. G. Cooper, P. V. Demarco, and D. O. Spry, *J. Am. Chem. Soc.*, **91**, 1528 (1969).

(7) See, e.g., G. Stork and J. Ficini, *J. Am. Chem. Soc.*, **83**, 4678 (1961); M. M. Fawzi and C. D. Gutsche, *J. Org. Chem.*, **31**, 1390 (1966).

(8) S. Kukolja and S. R. Lammert, *J. Am. Chem. Soc.*, preceding paper in this issue.

(9) Hydrolysis of the p-nitrobenzyl ester group under these conditions has been found to be generally applicable.

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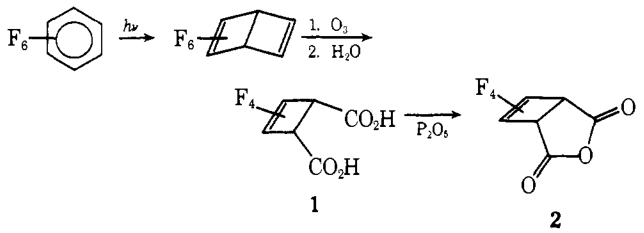
Tetrafluorocyclobutadiene

Sir:

The simplest perfluoroannulene occupies a place of special interest, particularly in light of the striking contrasts which set fluorocarbons apart from their hydrocarbon analogs.[1] We wish to report a synthesis of the short-lived tetrafluorocyclobutadiene,[2,3] whose intermediacy is revealed by its transformation and trapping products.

Hexafluoro(Dewar benzene), prepared by vapor-phase photoisomerization of hexafluorobenzene[4] at 2537 Å, was treated in methylene chloride solution with an equivalent of ozone at −18°. The solution was stirred for 24 hr with water at room temperature, and the aqueous phase was then evaporated in vacuo. Sublimation of the residue (0.1 mm, 100°) gave the powerfully acidic tetrafluorocyclobutene-3,4-dicarboxylic acid (**1**) as hygroscopic white crystals: mp 128–129°;[5] ir (KBr) 2.9–4.2 (br, ν(O—H)), 5.59 (m, ν(C=C)), 5.73 (s, ν(C=O)), 7.31 (s, ν(C—F)) μ; ^{19}F NMR (CD_3CN) δ 41.9, 86.7 (each t, 13 Hz band width);[6] ^{1}H NMR (CD_3CN) δ 9.7 (s). A mixture of the diacid with excess phosphorus pentoxide was heated at 130° and 50 mm. Anhydride **2** crystallized on the walls of a tube which projected vertically from the reaction vessel. Because it hydrolyzes readily to the diacid when exposed to air, the volatile anhydride was generally manipulated on a vacuum line. Resublimation gave **2** with the mp 104.5–105.5° (44% yield based on hexafluorobenzene): ir (CH_2Cl_2) 5.29 (w, ν(C=O), as), 5.49 (s, ν(C=O), sym), 5.65 (m, ν(C=C)), 7.36 (s, ν(C—F)) μ; ^{19}F NMR (CH_2Cl_2) δ 31.8, 101.8 (symmetrical sextets, band width 16 Hz); MS 196 (parent), 124 (base, $C_4F_4^+$).[7]

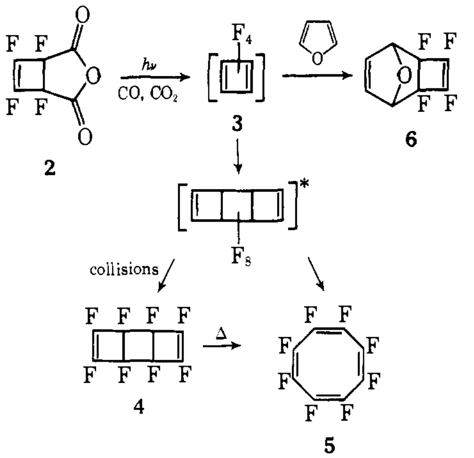


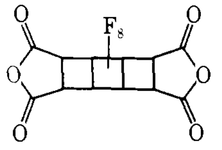
The anhydride was sublimed in vacuo into a quartz vessel and photolyzed in the vapor phase (<10 mm, ~50°) at 2537 Å in the presence of 500 mm of nitrogen.[8] Destruction of **2** was complete within 2.5 hr, and the volatile reaction products were vacuum-transferred to a U trap. A single highly volatile solid, octafluoro[4.2.0.0^{2,5}]cycloocta-3,7-diene (**4**), accounted for ~90% of this material (41% yield from **2**). Purified by gas chromatography, this fluorocarbon formed colorless crystals: mp 40–41.5°; ir (vapor) 5.67 (m, ν(C=C)), 7.23 (s, ν(C—F)) μ; ^{19}F NMR (CH_2Cl_2) δ 48.9, 105.1 (identical triplets with some fine structure, band width 10 Hz); MS 248 (parent). Its structure was confirmed by thermal isomerization (150°, 4 hr) to octafluorocyclooctatetraene (**5**).[9] The latter is also a volatile, colorless solid, mp 41–41.5°, whose narrow singlet at δ 45.0 in the ^{19}F spectrum betrays its high symmetry: ir (CH_2Cl_2) 5.80 (w, ν(C=C)), 5.91 (m, ν(C=C)), 7.50 (s, ν(C—F)) μ; MS 248 (parent). Interestingly, octafluorocyclooctatetraene is formed in good yield when **2** is photolyzed in the absence of nitrogen. Presumably the inert gas forestalls formation of **5** by collisionally deactivating the tricyclooctadiene,[10] which must be generated in high vibrational states.

Irradiation of **2** (<10 mm, ~50°) at 2537 Å in the presence of ~100 mm of furan yielded, in addition to **5**, a compound (**6**) having the composition of a 1:1 adduct of furan with tetrafluorocyclobutadiene. After purification by gas chromatography, **6** melted at 37–38.5° (10.5% yield): ir (vapor) 3.3 (w, ν(C—H)), 5.65 (m, ν(CF=CF)), 7.35 (s, ν(C—F)) μ; ^{19}F NMR (CH_2Cl_2) δ 46.8, 108.5 (doublets with fine structure, 8 and 9 Hz splitting, respectively); ^{1}H NMR (CH_2Cl_2) δ 5.53, 7.20 (narrow multiplets, ~3 and ~2 Hz h.h.w., respectively); MS 192 (parent).

The transformations described above, together with a mechanistic interpretation based on tetrafluorocyclobutadiene, are summarized in Scheme I. One might escape postulating perfluorocyclobutadiene by imagining **4** and **6** to arise via photocycloaddition of **2** to itself and to furan, giving **7** and **8**, respectively, followed by photoelimination of carbon monoxide and dioxide.[11] Several observations conspire to undermine this interpretation. They include the fact that (1) ample precedent exists for photofragmentation of cyclobutenedicarboxylic anhydrides to cyclobutadienes,[2] (2) our reaction conditions (gas phase, <10 mm) are conducive to fragmentation vis-a-vis dimerization of **2**, and (3) only a single stereoisomer of **4** and of **6** has been found, consistent with their origin in Diels–Alder reactions. Finally, photolysis of **2** (<10 mm, ~50°) at 2537 Å in the presence of ~100 mm of hexafluorocyclobutene led again to **4** and **5**, and no product incorporating the cyclobutene was found. Since the double bond of perfluorocyclobutene (which is present in ~ 15-fold excess) should be a good model for that in **2**, this result argues strongly against photodimerization of **2** in the above experiments. Our findings appear to require the intermediacy of perfluorocyclobutadiene.

Scheme I





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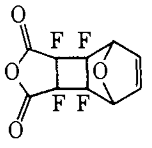

8

When **2** (<10 mm, ~50°) was irradiated at 2537 Å in the presence of ~100 mm of ethylene, acrylonitrile, or ethyl vinyl ether, **4** and/or **5** were produced but no trapping products were detected. Perfluorocyclobutadiene appears to be rather selective in the role of Diels–Alder diene.

Further studies of the cyclobutadiene, both in fluid media and in matrix isolation, are under way in our laboratory.

Acknowledgment. We wish to thank the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for generous financial support.

References and Notes

(1) See, for example, W. A. Sheppard and C. M. Sharts, "Organic Fluorine Chemistry", W. A. Benjamin, New York, N.Y., 1969, Chapters 1–3, 8.

(2) For an excellent review of cyclobutadiene chemistry, see G. Maier, *Angew. Chem., Int. Ed. Engl.*, **13**, 740 (1974).

(3) For especially elegant and revealing studies of cyclobutadiene and its deuterated derivatives in matrix isolation, see A. Krantz, C. Y. Lin, and M. D. Newton, *J. Am. Chem. Soc.*, **95**, 2744 (1973); O. L. Chapman, D. De La Cruz, R. Roth, and J. Pacansky, *ibid.*, **95**, 1337 (1973); O. L. Chapman, C. L. McIntosh, and J. Pacansky, *ibid.*, **95**, 614 (1973); A. Krantz and C. Y. Lin, *J. Chem. Soc., Chem. Commun.*, 1111 (1972).

(4) G. Camaggi and F. Gozzo, *J. Chem. Soc.*, 489 (1969); G. Camaggi, F. Gozzo, and L. Cevidalli, *Chem. Commun.*, 313 (1966); I. Haller, *J. Am. Chem. Soc.*, **88**, 2070 (1966).

(5) All melting points were measured in evacuated, sealed tubes and are uncorrected.

(6) ^{19}F chemical shifts are expressed in ppm upfield from external trifluoroacetic acid, which functioned as both reference and lock.

(7) Small impurity signals were present in this spectrum.

(8) Since traces of mercury vapor were present in this and the subsequently described experiments, the decomposition of **2** may have been mercury-sensitized in part. The anhydride shows substantial absorption at 2537 Å, however ($\lambda_{max}^{CH_3CN}$ 240 mm, ϵ 540), and photolysis with an unfiltered medium-pressure mercury arc ("reversed" 2537 Å line) also yields **4**.

(9) Thermal isomerization of the syn and anti dimers of cyclobutadiene itself is discussed by H. M. Frey, H. D. Martin, and M. Hekman, *J. Chem. Soc., Chem. Commun.*, 204 (1975); R. S. Case, M. J. S. Dewar, S. Kirschner, R. Pettit, and W. Slegeir, *J. Am. Chem. Soc.*, **96**, 7581 (1974).

(10) For other examples of this phenomenon see, e.g., D. R. Arnold, N. C. Baird, J. R. Bolton, J. C. D. Brand, P. W. M. Jacobs, P. deMayo, and W. R. Ware, "Photochemistry", Academic Press, New York, N.Y., 1974, Chapter 6.

(11) Direct photolysis of cyclic anhydrides is described by A. Zweig, K. R. Huffman, J. B. Gallivan, M. K. Orloff, and F. Halverson, *J. Am. Chem. Soc.*, **96**, 1449 (1974). For mercury-sensitized decomposition, see I. S. Krull and D. R. Arnold, *Tetrahedron Lett.*, 4349 (1969).

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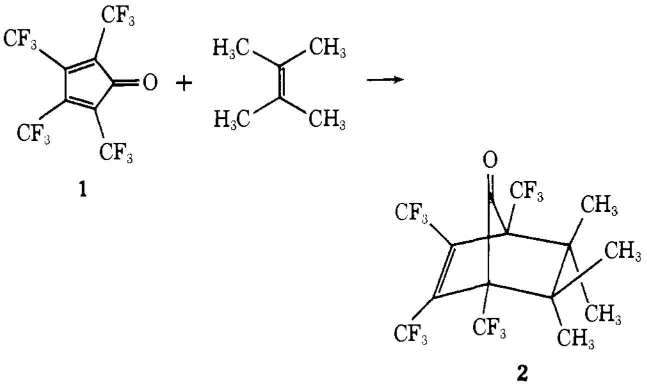
Perfluorotetramethylcyclopentadienone as a Diels-Alder Diene

Sir:

Largely ignored since its discovery and characterization by Wilkinson's group in the early 1960's,[1,2] perfluorotetramethylcyclopentadienone (**1**) is nonetheless a remarkable compound. This highly volatile yellow solid is stable as a monomer, apparently by virtue of the bulk of its trifluoromethyl substituents.[3] Its resistance to dimerization disguises the fact that **1** is an extremely reactive molecule, one aspect of whose multifaceted chemistry provides the substance of this report.

When petroleum ether solutions of the dienone and tetramethylethylene are combined, a deep burgundy color attributable to π-complexation[4] develops immediately but fades upon standing at room temperature. Removal of the solvent gives the Diels-Alder adduct **2** in excellent yield.



1

2

The structure of **2** is established by its microanalysis, ^{19}F and ^{1}H NMR spectra (Table I), high-frequency carbonyl stretching absorption (1825 cm^{-1}, CCl_4),[5] and an ultraviolet maximum at 235 nm (ϵ 903, cyclohexane) attributable to the homoconjugated enone chromophore. Diels-Alder addition of **1** to ethylene is much faster, presumably for steric reasons (k = 0.3 l. mol^{-1} sec^{-1} in dioxane, 28°). This rate is virtually identical with that of the reaction between ethylene and dimethyl *sym*-tetrazinedicarboxylate, a super "diene" in the "Diels-Alder reaction with inverse electron demand".[6]

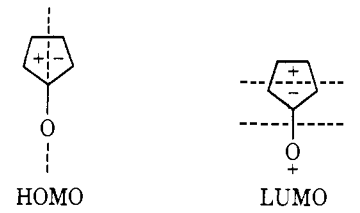
More vigorous conditions are required for reaction of **1** with conventional dienophiles, but dimethyl maleate and fumarate, for example, add readily and stereospecifically at 120°. The reactions yield a single cis and the trans diester, respectively.[7] Table I also contains adducts obtained from several other olefins.[8]

Acetylene adds to **1** rapidly even below room temperature, yielding, after spontaneous extrusion of carbon monoxide, perfluoro-1,2,3,4-tetramethylbenzene. Again, the reaction is general for acetylenes; e.g., dimethyl acetylenedicarboxylate gives the expected phthalate in excellent yield at 120°.

Attack of dienone **1** on conjugated dienes was explored in order to learn which component would assume the diene role in the Diels-Alder addition. In very facile reactions with 1,3-cyclohexadiene, furan, and cyclopentadiene, the dienone played that part in every case (see Table I).

When naphthalene and **1** are combined, the green charge transfer complex[2] slowly disappears even at 80° with the formation, in high yield, of a mixture of 1:2 adducts. Not surprisingly, attempts to obtain adducts with benzene, which gives an orange charge-transfer complex,[2] have failed.[9]

Cyclopentadienones owe their great reactivity principally to a low-lying LUMO and the consequently narrow gap between frontier molecular orbitals.[10] The four powerfully electron-withdrawing trifluoromethyl groups of dienone **1** should increase the effective Coulomb integral at the attached ring carbons, thus dropping both HOMO and LUMO energies below those of the parent molecule. The gap between them should widen somewhat since the HOMO encompasses only these carbons while the LUMO has substantial coefficients at all six skeletal atoms. Indeed, the long-wavelength uv maximum of **1** (340 nm, CCl_4[2]) is consistent with this surmise (cf. that of 3-*tert*-butylcyclopentadienone: 380 nm, isooctane[10]). More important for explaining the special properties of **1** is the fact that the LUMO, which is "bonding" even in the parent dienone



(HMO approximation[11]), must lie extraordinarily low. Hence, the perfluorodienone's enthusiasm for charge-transfer complex formation and cycloaddition with donor π-systems is easily understood.

The regiochemistry of the reactions of **1** with dienes runs counter to the clear prediction from simple molecular orbital theory that the dienone should function as the dienophile.[10,12] Theory gains credence from the finding that cyclopentadienone itself behaves as expected toward cyclopentadiene.[13] Examination of models suggests that the aberrant behavior of **1**, which is shared by other highly substituted cyclopentadienones.[3] is determined by steric interactions in the Diels-Alder transition states.