Studies on Organic Fluorine Compounds.[1] 36. Synthesis and Reactions of Trifluoromethylated Diphosphabenzvalene[2]

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Photolysis of 2,3,5,6-tetrakis(trifluoromethyl)-1,4-diphosphabenzene (3) or its precursor 2 gave 1,3,4,6-tetrakis(trifluoromethyl)-2,5-diphosphatricyclo[3.1.0.0^{2,6}]hex-3-ene (4), the first isolated analogue of benzvalene containing heteroatoms in its ring system. Compound 4 reacted with dienes or phenyl azide as a dienophile or a dipolarophile.

Introduction

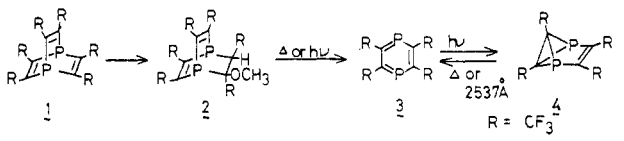
Scrambling and valence bond isomerization reactions of aromatic compounds have been thoroughly studied, and some valence bond isomers were postulated as intermediates in scrambling reactions. Further, Dewar benzene, prismane, and benzvalene and their derivatives have been synthesized and reactions of these compounds have been investigated.[3] Participation of such valence bond isomers in the photoscrambling reactions of heteroaromatic compounds has also been proposed.[4] Since then Dewar-type and prismane-type isomers of heteroaromatic compounds having fluorine and/or perfluoroalkyl substituents were isolated.[5] However, benzvalene analogues of heteroaromatic compounds have never been isolated or observed spectroscopically.[6] We now report the first example of a heterocyclic benzvalene. Thus, 1,3,4,6-tetrakis(trifluoromethyl)-2,5-diphosphatricyclo[3.1.0.0^{2,6}]hex-3-ene (4) was obtained by photolysis of 2,3,5,6-tetrakis(trifluoromethyl)-1,4-diphosphabenzene (3),[7] which was formed from the methanol adduct of 2,3,5,6,7,8-hexakis(trifluoromethyl)-1,4-diphosphabicyclo[2.2.2]octa-2,5,7-triene (1). Some reactions of 4 will be also described (see Scheme I).

Results and Discussion

1. Synthesis of 1,3,4,6-Tetrakis(trifluoromethyl)-2,5-diphosphatricyclo[3.1.0.0^{2,6}]hex-3-ene (4). Photolysis of many fluorine-containing heterocyclic compounds resulted in scrambling reactions, such as photoisomerization of perfluoropyridazine to the corresponding pyrimidine, and in special cases, their valence bond isomers were isolated. Therefore, we tried the photoisomerization of 3, which was a new ring system and had fluorine substituents.

Irradiation of a solution of 3 in perfluoropentane with a high-pressure mercury lamp gave a colorless oil (4), which solidified when cooled in an acetone–dry ice bath. The molecular ion of 4 showed that it was an isomer of 3. The presence of a double bond was confirmed by an absorption at 1620 cm^{-1} in the IR spectrum. Two kinds of trifluoromethyl groups of equal intensity were observed at −10.2 and −6.0 ppm in the ^{19}F NMR spectrum, as shown in Figure 1. The first peak appeared as an apparent doublet

Scheme I



with a complex multiplet structure of AA'X$_3$X$_3$', which shows that the relation between A(P) and X$_3$(F$_3$) is different from that between A' and X$_3$. The second appeared as an apparent triplet, which show that X$_3$ couples with A as with A'. Only one kind of phosphorus atom was observed in the ^{31}P NMR spectrum. These spectral data showed that 4 was 1,3,4,6-tetrakis(trifluoromethyl)-2,5-diphosphatricyclo-[3.1.0.0^{2,6}]hex-3-ene. Further, the ^{19}F-decoupled ^{13}C NMR spectrum of 4 showed two absorptions at 71.17 and 161.25 ppm (Figure 2). The latter signal was assigned to the sp^2 carbon bound to a phosphorus atom by comparison with the sp^2 carbon of 3 (163.9 ppm). The pattern of this multiplet might be due to coupling with two different phosphorus atoms in an AA'X system. The high-field triplet was assigned to the sp^3 carbons bound to two phosphorus atoms in an equivalent environment, as in an A$_2$X system.

Compound 4 was stable at room temperature and was not attacked by oxygen but was slowly isomerized to 3 on heating; the half-life of 4 at 198 °C in perfluorobenzene was about 75 min. Further, irradiation of 4 with a low-pressure mercury lamp (2537 Å) caused the decomposition of 4 through 3. Transient formation of the latter was observed by ^{19}F NMR spectroscopy. Compound 4 was also formed by irradiation of 2 with a high-pressure mercury lamp. Thus, 2 was photochemically cleaved to 3 and 1,1,1,4,4,4-hexafluoro-2-methoxybut-2-ene, the former of which was converted to 4.

Compound 4 is the first example of a benzvalene analogue containing heteroatoms in the ring system. Photolysis of the nitrogen analogue of 4, tetrakis(trifluoromethyl)pyrazine, did not give any valence bond isomers. Therefore, the formation and the stability of 4 might be due to the special properties of excited phosphorus atoms, the longer P–C bond, and/or the difference in hybridization between first and second row elements. That the last factor is important was suggested by the fact that photolysis of tetrakis(trifluoromethyl)thiophene gave a Dewar-type isomer while that of tetrakis(trifluoromethyl)furan did not. The trifluoromethyl groups must have contributed to the stability of 4. Irradiation of 3 with a low-pressure mercury lamp caused the signals of 3 to disappear slowly, while some other peaks different from those of 3 or 4 were transiently observed. This suggests that other valence bond isomers of 3 are very unstable even if formed. We are now studying the synthesis of these isomers at low temperature.

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(3) E. E. van Tamelen, S. P. Pappas, *J. Am. Chem. Soc.*, **84**, 3789 (1962).
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(5) (a) M. G. Barlow, R. N. Haszeldine, and J. G. Dingwall, *J. Chem. Soc., Perkin Trans. 1*, 1542 (1973); (b) Y. Kobayashi and A. Ohsawa, *Tetrahedron Lett.*, 2643 (1973).
(6) R. D. Chambers, J. A. H. MacBride, J. R. Maslakiewicz, and K. C. Srivastava, *J. Chem. Soc., Perkin Trans. 1*, 396 (1975).
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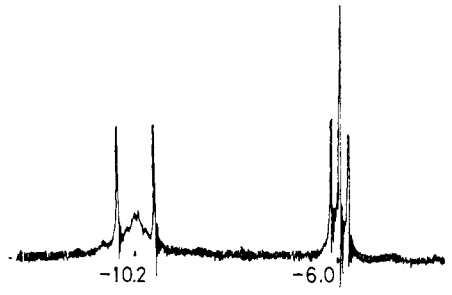


Figure 1. ^{19}F NMR spectrum of 4.

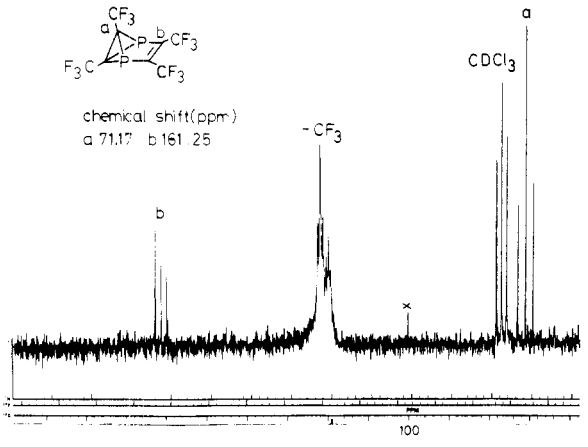
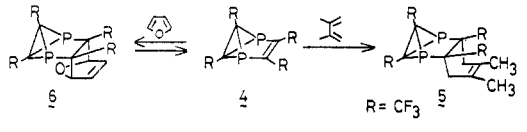


Figure 2. ^{19}F-Decoupled ^{13}C NMR spectrum of 4 at 25.1 MHz.

Scheme II



2. Reactions of 4. At first we tried to compare the reactivity of the olefinic part of 4 with that of the benzene analogue, hexakis(trifluoromethyl)benzvalene, which is known to react with dienes and 1,3-dipolar compounds.[8]

The Diels–Alder reaction of 4 with 2,3-dimethyl-1,3-butadiene afforded adduct 5 and with furan the adduct 6, whose stereochemistry was assumed to be exo in the analogy with that of the benzvalene adduct. While adduct 5 was stable at room temperature, 6 was in equilibrium with 4 and furan in solution. Thus, solution of the adduct 6 in *n*-pentane caused the appearance of 4 as observed in the ^{19}F NMR spectrum. This equilibrium was very fast at 70 °C (see Scheme II).

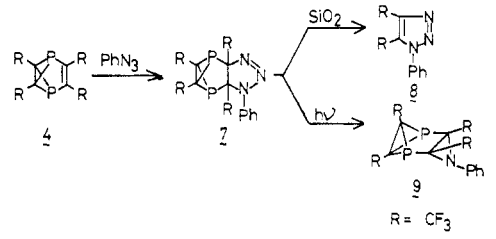
Treatment of 4 with phenyl azide in pentane gave a 1,3-dipolar cycloadduct (7). Treatment of 7 with silica gel gave a triazole (8). The fate of the diphosphabicyclobutane part is not still clear. Photolysis of 7 caused loss of a nitrogen molecule to give an aziridine (9) (see Scheme III).

We expected that thermolysis of 7 would give the diazoimine 10 or the diphosphazepine 11, which would be formed through skeletal rearrangement of 10 to eliminate the internal strain. However, thermolysis of 7 at 140 °C gave 9 and the retroreaction product 4, the former possibly having been formed by internal insertion of the carbene into the C–N double bond (Scheme IV).

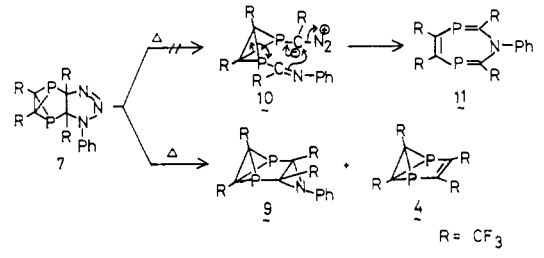
Experimental Section

1,3,4,6-Tetrakis(trifluoromethyl)-2,5-diphosphatricyclo-[3.1.0.0^{2,6}]hex-3-ene (4). A. By Irradiation of 3. A solution of 3, which was obtained in situ by thermolysis of 2 in *n*-hexane,

Scheme III



Scheme IV



evaporation of the solvent, and solution of the residue in perfluoropentane in an argon atmosphere, was sealed in a Pyrex tube under vacuum and irradiated with a high-pressure mercury lamp for 72 h. The yellow reaction mixture was distilled by trap-to-trap distillation in vacuo, and 4 was obtained in a trap cooled in a CCl_4–CO_2 bath (volatile colorless oil). Pure 4 solidified at −78 °C: IR (*n*-pentane) 1620, 1100–1300 cm^{-1}; ^{19}F NMR (*n*-pentane) −10.2 (6 F, d, 0.5(J_{PF} + $J_{P'F}$) = 22.6 Hz), −6.0 (6 F, t, J_{PF} = 5.2 Hz) ppm;[9] ^{31}P NMR ($CDCl_3$) −17.96 (singlet by irradiation of fluorine) ppm;[10] ^{13}C NMR ($CDCl_3$) δ 71.17 (t, J_{PC} = 47.5 Hz), 119.1–123.0 (m, CF_3), 161.25 (m); mass spectrum, *m/e* 386 (M^+); high-resolution mass spectrum, calcd for $C_8F_{12}P_2$ 385.928, found 385.929.

B. By Irradiation of 2. A solution of 2 (1.00 g) and perfluoropentane (5 mL), sealed in vacuo in a Pyrex tube, was irradiated with a high-pressure mercury lamp at room temperature for 72 h. Initially insoluble 2 slowly dissolved during irradiation. 4 (273 mg, 41% based on 2) was obtained by the same treatment as described in A.

Reaction of 4 with Furan. A solution of 4 (85.7 mg) and furan (50 mg) in *n*-pentane (0.5 mL) was stirred for 5 days at room temperature. After removal of furan and solvent on a vacuum line, sublimation [50–60 °C (3 mmHg)] of the residue gave 53.5 mg (53 %) of 6: colorless cyrstals; mp 66–70 °C dec; IR (*n*-pentane) 1100–1300 cm^{-1}; ^{19}F NMR ($CDCl_3$) −10.8 (6 F, d, J_{PF} = 31.6 Hz), −8.8 (6 F, m) ppm; ^1H NMR ($CDCl_3$) 5.18 (2 H, br s), 6.6 (2 H, s) ppm; mass spectrum, *m/e* 386 (M^+ − furan), 68 (furan). Anal. Calcd for $C_{12}H_4OP_2F_{12}$: C, 31.74; H, 0.89; F, 50.21. Found: C, 31.59; H, 1.00; F, 50.13.

Reaction of 4 with 2,3-Dimethyl-1,3-butadiene. A solution of 4 (128 mg) and 2,3-dimethyl-1,3-butadiene (54 mg) in *n*-pentane was stirred for 70 h at room temperature. After removal of 2,3-dimethyl-1,3-butadiene and solvent on a vacuum line, bulb-to-bulb distillation [122–124 °C (16 mmHg)] of the residue gave 8,9-dimethyl-1,3,4,6-tetrakis(trifluoromethyl)-2,5-diphosphatetracyclo[4.4.0.0^{2,4}.0^{3,5}]dec-8-ene (5) as a pale yellow oil (93.6 mg 60%) which crystallized on standing: mp 55–56 °C; IR (*n*-pentane) 1100–1300 cm^{-1}; ^{19}F NMR ($CDCl_3$) −9.2 (6 F, m), −3.2 (6 F, d, J_{PF} = 22.6 Hz) ppm; ^1H NMR ($CDCl_3$) 1.82 (6 H, s), 2.5 (4 H, m) ppm; mass spectrum, *m/e* 468 (M^+); high-resolution mass spectrum, calcd for $C_{14}H_{10}F_{12}P_2$ 468.007, found 468.008.

Reaction of 4 with Phenyl Azide. A solution of 4 (227 mg) and phenyl azide (70 mg) in *n*-pentane was sealed in a Pyrex tube under vacuum and kept at 50 °C for 2 days. After removal of solvent on a vacuum line, bulb-to-bulb distillation [70 °C (7 mmHg)] of the residue gave 9-phenyl-1,3,4,6-tetrakis(trifluoromethyl)-2,5-diphospha-7,8,9-triazatetracyclo[4.3.0.0^{2,4}.0^{3,5}]non-7-ene (7) as a pale yellow oil (124.5 mg, 41.7%): IR (CH_2Cl_2) 1595,

(8) (a) Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Hanzawa, and M. Honda, *Tetrahedron Lett.*, 2545 (1976); (b) *ibid.*, 3001 (1975).

(9) Benzotrifluoride as an internal standard.
(10) 85% H_3PO_4 as an external standard.

1480, 1100–1300 cm^{-1}; ^{19}F NMR ($CDCl_3$) −10.8 (3 F, m), −10.0 (3 F, m), −5.2–2.8 (6 F, m) ppm; ^{1}H NMR ($CDCl_3$) 7.5 (s) ppm; mass spectrum, m/e 477 ($M^+ - N_2$); high-resolution mass spectrum, calcd for $C_{14}H_5F_{12}P_2N_3$ 476.970, found 476.969.

Irradiation of 7. After irradiation of **7** in *n*-pentane with a high-pressure mercury lamp for 4 h, the solvent was evaporated under vacuum. Bulb-to-bulb distillation [60–65 °C (5 mmHg)] of the residue gave 7-phenyl-1,3,4,6-tetrakis(trifluoromethyl)-2,5-diphospha-7-azatetracyclo[4.1.0.0^{2,4}.0^{3,5}]heptane (**9**) as a pale yellow oil (63% estimated by ^{19}F NMR): IR ($CHCl_3$) 1595, 1490, 1100–1300 cm^{-1}; ^{19}F NMR ($CDCl_3$) −7.2 (3 F, m), −6.0 (3 F, m), −2.8 (6 F, d, J_{PF} = 21.4 Hz) ppm; ^{1}H NMR ($CDCl_3$) 6.9–7.7 (aromatic) ppm; mass spectrum, m/e 477 (M^+); high-resolution mass spectrum, calcd for $C_{14}H_5F_{12}P_2N$ 476.970, found 476.969.

Thermolysis of 7. A solution of **7** in *n*-pentane was sealed in a Pyrex tube under vacuum and heated at 140 °C for 8 h. ^{19}F NMR spectrum of this mixture indicated the formation of **9** and **4**, the latter of which might be formed by retro 1,3-dipolar reaction.

1-Phenyl-4,5-bis(trifluoromethyl)-1,2,3-triazole (8). Compound **7** was chromatographed on silica gel TLC plate, using ether–*n*-pentane (1:6) as eluant. Extraction of the fluorescent zone by a UV lamp gave the triazole **8**.[11]

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Registry No. 2, 62218-18-2; **3**, 62218-19-3; **4**, 65114-90-1; **5**, 74930-70-4; **6**, 74930-71-5; **7**, 74930-72-6; **9**, 74930-73-7; 2,3-dimethyl-1,3-butadiene, 513-81-5; phenyl azide, 622-37-7; furan, 110-00-9.

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Isolation and Structure of the Novel Branched-Chain Amino Sugar Derived from Antibiotic A35512B[1]

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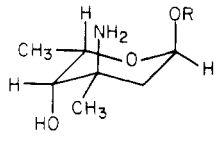
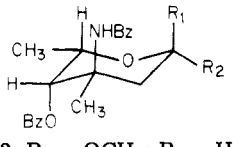
Methanolysis of glycopeptide antibiotic A35512B with 1.5 N HCl (methanol) gave a new 2,3,6-trideoxy amino sugar. The structure of this amino sugar was determined by NMR and CD techniques and shown to be 3-amino-2,3,6-trideoxy-3-*C*-methyl-L-*xylo*-hexopyranose, **1**. This structure determination was carried out on the *N,O*-dibenzoyl anomeric methyl glycosides **3** and **5**. Amino sugar **1** was shown to be the C-3 epimer of L-vancosamine.

A35512B is a new gram-positive antibiotic which was recently isolated by Michel and Shah from an actinomycete, *Streptomyces candidus*.[2] Comparative chromatographic behavior indicated that A35512B belonged to the glycopeptide family of antibiotics and therefore was related to vancomycin, ristocetin, avoparcin, and others.[3]

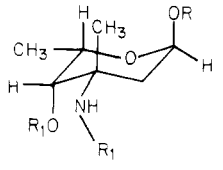
Johnson[4] and also Williams[5] reported that an amino sugar, L-vancosamine (**6**), was a constituent part of the glycopeptide vancomycin. Similarly, several other glycopeptides have since been shown to have an amino sugar as an integral part of their structure.[6–8] In this paper we report the isolation, structure, and stereochemistry of **2**,



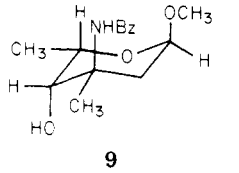
1, R = H
2, R = CH_3



3, R_1 = OCH_3; R_2 = H
4, R_1 = OH; R_2 = H
5, R_1 = H; R_2 = OCH_3



6, R = R_1 = H (L-vancosamine)
7, R = CH_3; R_1 = H
8, R = CH_3; R_1 = Bz



9

a novel amino sugar constituent of glycopeptide antibiotic A35512B.

Results and Discussion

Methanolysis of A35512B (1.5 N HCl, reflux 18 h) produced a peptide (aglycon) which precipitated from solution when the pH was adjusted to 7–8. The filtrate which contained the liberated neutral and basic fragments was passed through a cation-exchange column (NH_4^+). An aqueous wash removed the neutral methyl glycosides. A stepwise elution with NH_4OH solution (0.5–3 N NH_4OH) gave a product mixture which was purified further by cellulose column chromatography (*n*-butanol, saturated

(1) This work was presented at the 17th Conference on Antimicrobial Agents and Chemotherapy, New York, NY, Oct 14, 1977.
(2) K. Michel, R. M. Shah, and R. L. Hamill, "A35512, A Complex of New Antibacterial Antibiotics Produced by *Streptomyces candidus* II. Isolation and Characterization", 17th Conference on Antimicrobial Agents and Chemotherapy, New York, NY, Oct 14, 1977, Abstract 41.
(3) For a review of both the chemical and biological properties of glycopeptide antibiotics, see H. R. Perkins and M. Nieto, *Ann. N. Y. Acad. Sci.*, **235**, 348 (1974).
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(8) J. J. Hlavka, P. Bitha, J. H. Boothe, and G. Morton, *Tetrahedron Lett.*, 175 (1974).
(9) See ref 4 and 6 for examples of the NMR properties and anomers of amino sugars of the general type studied here.

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