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Studies on Organic Fluorine Compounds. XIX.*,1) Synthesis and Reactions of "Dewar" Thiophene2)

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The structure of photo isomer of 2,3,4,5-tetrakis(trifluoromethyl)thiophene (I) was determined as "Dewar" type (II) by ^{13}C-NMR (nuclear magnetic resonance) and other physical and chemical data. Diels-Alder reaction of II with furans gave *exo-exo* type products, 10-oxa-4-thiatetracyclo[5.2.1.0^{2,6}.0^{3,5}]dec-8-ene derivatives (VI), which was derived to substituted oxahomocubanes, 9-oxapentacyclo[4.2.1.0.^{2,5}0^{3,8}.0^{4,7}]nonanes (VIII) by successive desulfurization and photochemical reactions.

The compound 2,3,4,5-tetrakis(trifluoromethyl)thiophene (I) is of interest, since it is known that some aromatic compounds with trifluoromethyl groups give fairly stable valence bond isomers4) on photoisomerization. We studied the photoisomerization of I and established the structure of the product to be the "Dewar" thiophene (II) from physical and chemical data. We also report here the results of investigation on the chemical properties of II and derivation of oxahomocubanes2) from II utilizing its high dienophilicity by the high strain of the ring system and strong electronegativity of the substituents, together with the high reactivity of II owing to the thiirane ring.

Irradiation of I (Synthesis of "Dewar" Thiophene)

It is well known that substituted thiophenes give position isomers by photorearrangement, and some valence bond isomers, *i.e.*, "Dewar" type (A in Chart 1), cyclopropenylthioketone type (C), and/or dipolar type (D) are postulated as intermediates in those cases.5) On the other hand, none of the valence bond isomers (A through E in Chart 1) had been isolated as stable isomers until 1970, when Heicklen, *et al.* investigated the photolysis of I at 2139Å or with Hg sensitization at 2537Å and obtained the isomer of I. At first they assigned the structure of the isomer to "Dewar" type6) (A), next to cyclopropenylthioketone type7) (C), and again to A type.8) (In Chart 1, all the substituents are trifluoromethyl groups.) Thus, their

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* Dedicated to the memory of Prof. Eiji Ochiai.

1) Part XVIII: Y. Kobayashi, I. Kumadaki, Y. Hanzawa, and M. Mimura, *Chem. Pharm. Bull.* (Tokyo), 23, 2044 (1975).

2) Preliminary communication: Y. Kobayashi, I. Kumadaki, A. Ohsawa, and Y. Sekine, *Tetrahedron Letters*, **1974**, 2841. Presented at the 93rd Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1973, and at the 6th Symposium on Heterocyclic Compounds, Nagoya, November 1973.

3) Location: *Kitashinjuku 3-chome, Shinjuku-ku, Tokyo.*

4) *a*) M.G. Barlow, R.N. Haszeldine, and R. Hubbard, *J. Chem. Soc.*, (*C*), **1970**, 1232; *b*) D.M. Lemal, J.V. Staros, and V. Austel, *J. Am. Chem. Soc.*, **91**, 3337 (1969); *c*) Y. Kobayashi, A. Ohsawa, and M. Baba, Abstract of The 5th Symposium on Heterocyclic Chemistry, Gifu, 1972, p. 1.

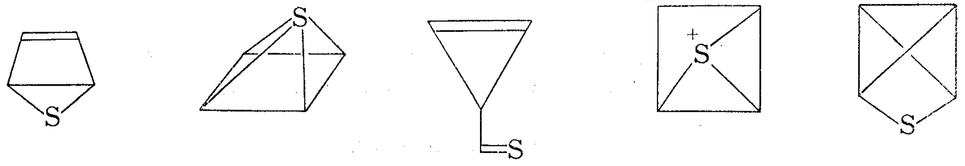
5) *a*) E.E. van Tamelen and T.H. Whitesides, *J. Amer. Chem. Soc.*, **93**, 6129 (1971); *b*) H. Wynberg, *Acc. Chem. Res.*, **4**, 65 (1971); *c*) R.M. Kellogg, *Tetrahedron Letters*, **1972**, 1428; *d*) A. Couture and A.L-Combier, *Tetrahedron*, **27**, 1059 (1971); *e*) E.E. van Tamelen, *Acc. Chem. Res.*, **5**, 186 (1972) and refs. therein.

6) S. Braslavsky, H.A. Wiebe, and J. Heicklen, Center for Air Environment Studies. Publication No. 164—170, Penn. St. Univ. (1970).

7) E.C. Wu and J. Heicklen, *J. Am. Chem. Soc.*, **93**, 3432 (1971).

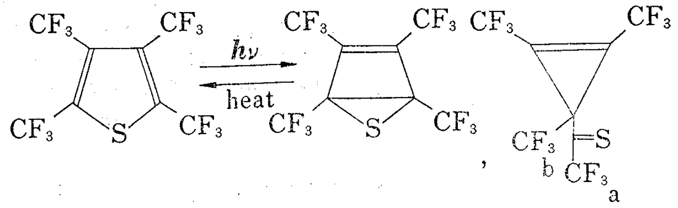
8) H.A. Wiebe, S. Braslavsky, and J. Heicklen, *Can. J. Chem.*, **50**, 2721 (1972).

assignment is not decisive about the structure and we considered its determination was necessary. We investigated the photolysis of I at 2537Å without sensitizer and improved the method of preparing the desired isomer (II) by the examination of photolysis conditions.



A B C D E

Chart 1



I II III

Chart 2

When I was irradiated at room temperature in a liquid phase (without a solvent) in a quartz flask by a low pressure mercury lamp under exclusion of air, the products were II and polymeric products of high boiling point, besides some recovery of I. In this method, though II was easily isolated by preparative gas–liquid chromatography (GLC), the yield of II was not satisfactory (22%), and a considerable amount of polymers was obtained. Formation of the polymers may have resulted from the intermolecular reaction of I and/or II. To avoid this polymerization, the photolysis was carried out in a gas phase at low pressure and the products were collected in a cold trap connected to the irradiation flask. In this case, only a small amount of polymers was formed and simple vacuum trap-to-trap distillation gave a fairly good yield of II (57.8%). This procedure is suitable for preparing II on a large scale. The isomer (II) is a pale yellow oil of high volatility and stable enough to be kept at room temperature. Mass spectrum of II showed the molecular peak (M^+) at *m/e* 356. In ^{19}F-NMR (nuclear magnetic resonance), II showed two signals of the same intensity at δ -0.88 and 2.15 (in carbon tetrachloride), the signal of benzotrifluoride being δ 0 as an internal standard, which suggests that II has two sets of equivalent trifluoromethyl groups with a symmetrical structure of A or E.

Infrared (IR) spectrum of II showed an absorption of the double bond substituted with trifluoromethyl groups at 1700 cm^{-1}, suggesting that the structure is A type, *i.e.*, 1,2,3,4-tetrakis(trifluoromethyl)-5-thiobicyclo[2.1.0]pent-2-ene.

However, Heicklen, *et al.*[7] assigned the structure of their isomer to C type (III), although the physical data were quite similar to ours; the small possibility, where chemical shifts in ^{19}F-NMR of trifluoromethyl groups (a and b) in the structure III are overlapping with each other, seemed to remain still. Therefore, we examined the ^{13}C-NMR of II. Signals of only two kinds of trifluoromethyl carbons were observed at δ 118.76 ($J_{C-F}=271.5$ Hz) and 122.96 ($J_{C-F}=273$ Hz). As it is very unlikely that the chemical shifts in ^{19}F- and ^{13}C-NMR and the coupling constants of a and b groups in III were all identical, the structure III can be excluded and it was shown that the structure of the isomer must be the "Dewar" type (II).

It is known that the trifluoromethyl group stabilizes valence bond isomers of benzene and pyridine,[4] as memtioned before. In this case, the trifluoromethyl group seems to stabilize II. Although substituted thiophenes are usually presumed to undergo photoisomerization through intermediates (C and/or D) different from A, isolation of II might indicate the possibility of another mechanism through type A intermediate. However, we cannot exclude this as a special case; presence of the trifluoromethyl group caused photoisomerization different from the usual cases.

Isomerization and Dimerization of II

The isomer II was converted to I in a quantitative yield by heating and the rate of conversion was first-order and independent of various solvents. Half-life at 160° was 5.1 hr (observed in benzene). When II was dissolved in dimethyl suloxide or dimethylformamide, crystals (IV) precipitated immediately. Compound IV shows two signals of the same intensity in ^{19}F-NMR and M^+ peak at *m/e* 712 and $C_8S_2F_{12}$ at 386 in mass spectrum, and an absorption of the cyclobutenic double bond substituted with trifluoromethyl groups at 1700 cm^{-1} in IR spectrum. These data are explained reasonably by the structure (IV) (Chart 3), while its stereochemistry (*endo* or *exo*) is not determined yet.

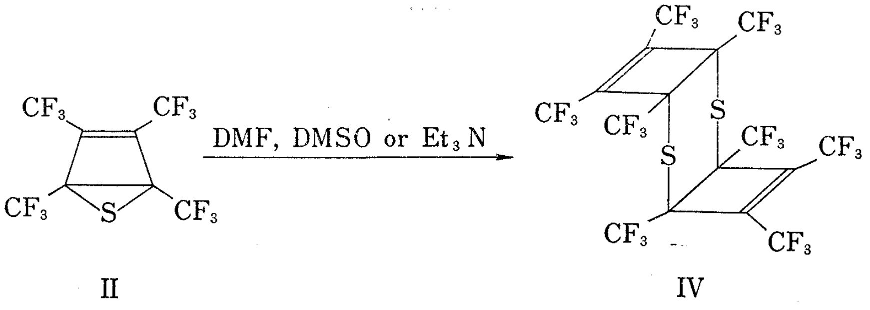


Chart 3

Derivation of Oxahomocubanes from II

As it is already known that the double bond in a cyclobutene ring substituted with trifluoromethyl groups sometimes undergoes Diels-Alder addition with electron-rich dienes,[9] we tried the Diels-Alder reaction of II with furans intending to employ II as a starting material of synthetic chemistry and to reconfirm its structure chemically at the same time. The compound II reacted with furan (Va) at room temperature to give an adduct (VIa). VIa showed two signals (δ 5.40 and 6.61, relative intensity 1:1) in ^{1}H-NMR and two signals (δ -7.50 and -2.33, relative intensity 1:1) in ^{19}F-NMR. Mass spectrum of VIa showed the M^+ at *m/e* 424. The absorption attributable to the cyclobutenic double bond near 1700 cm^{-1} was absent in IR spectrum of this adduct. These data suggest that the double bond of II reacted with Va to give a one-to-one adduct of symmetrical structure. Further, we chose the following substituted furans, tetramethylfuran (Vb) and 3,4-bis(trifluoromethyl)-2,5-diethylfuran (Vc), as dienes to examine the substituent effects of furan. Vc did not give any adduct, while Vb gave a similar adduct (VIb). This fact might show that the methyl groups in Vb did not inhibit the addition reaction, but the trifluoromethyl groups in Vc did; namely, the electron-attracting character of trifluoromethyl groups on the furan ring seems to be more important than the steric effect of methyl groups in this addition reaction. Treatment of VIa with triphenylphosphine caused desulfurization from the thiirane part to give a product (VIIa). The absorption at 1718 cm^{-1} in IR spectrum of VIIa shows that a double bond substituted with trifluoromethyl group was introduced. While the signal of olefinic protons was observed at a similar position as in VIa, the signal of two protons on the carbons constituting the ether linkage shifts from δ 5.44 to δ 4.89 by this desulfurization.

Although this fact suggests that the cyclobutene ring is *exo* to the furan moiety, the stereochemistry concerning the thiirane ring was still unknown. The whole structure of VIb was established by X-ray analysis[10] as shown in Chart 4. This shows that the Diels-Alder reaction gave *exo-exo* adducts, possibly because of the steric requirements in a transition state.

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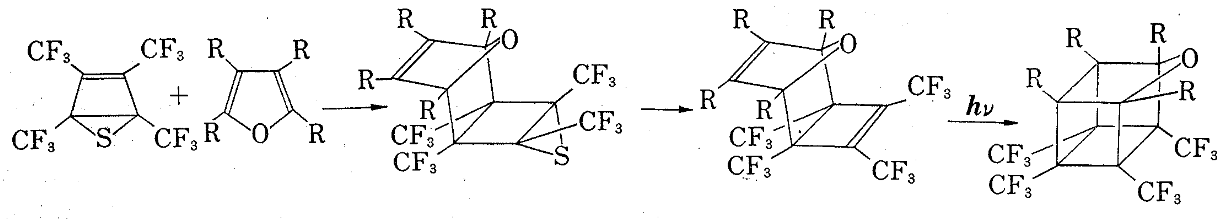
9) *a*) M.G. Barlow, R.N. Haszeldine, and R. Hubbard, *Chem. Commun.*, **1969**, 301; *b*) *Idem*,. *J. Chem. Soc.* (*C*), **1971**, 90.

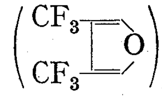
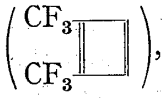
10) N. Kikutani, Y. Iitaka, Y. Kobayashi, I. Kumadaki, A. Ohsawa, and Y. Sekine, *Acta Cryst.*, **B 31**, 1478 (1975).



a : R=H
b : R=CH$_3$

Chart 4

VIIb was also formed from VIb by a treatment similar to the above.

Irradiation of VIIa in acetonitrile in a quartz tube at −10° by a low pressure mercury lamp gave a product (VIIIa), which showed no double bond absorption in IR spectrum, two signals (δ 3.69 and 5.64, relative intensity 1: 1) in ^{1}H-NMR, and two signals of the same intensity in ^{19}F-NMR. Massspectrum of VIIIa showed m/e 392 (M$^+$), 204 , 188 , and 68 (furan$^+$). From these data the structure of VIIIa was determined as 2,3,4,5-tetrakis(trifluoromethyl)-9-oxapentacyclo-[4.2.1.0.^{2,5}0.^{3,8}0.^{4,7}]nonane. Similarly, VIIb gave oxahomocubane (VIIIb) by the same treatment (Chart 4).

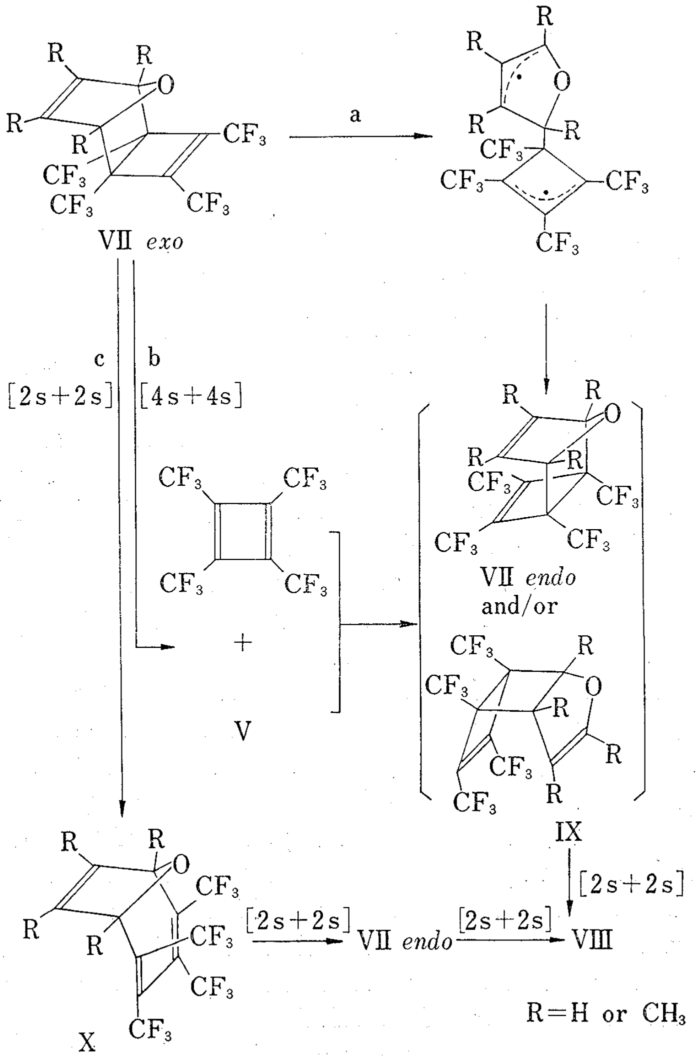


Chart 5

It might be considered that a photoisomerization process VII *exo* to VII*endo* or VII*exo* to IX takes place in the reaction as suggested by Eberbach, *et al.*[11] (path a or b) for the synthesis of other types of oxahomocubanes using benzophenone as a sensitizer. In our case, as addition of 1,3-pentadiene did not retard the photocyclization and addition of benzophenone retarded this reaction, the path b by Eberbach or a process *via* bicyclo intermediate (X) giving VII *endo* (path c) seems to be more probable than path a (Chart 5).

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[11] *a*) W. Eberbach and M.P-Argueilles, *Chem. Ber.*, **105**, 3078 (1972); *b*) E. Haselbach and W. Eberbach, *Helv. Chim. Acta.*, **56**, 1944 (1973).

Experimental

Photolysis of Tetrakis(trifluoromethyl)thiophene (I)——a) Without Solvent; I (8.30 g) was sealed in a 500 ml quartz tube *in vacuo* and irradiated with a low pressure mercury lamp for 150 hr with occasional shaking. The product was separated by preparative GLC. (Shimazu GC–1C. Column: DEGS, ϕ 17 mm, l 35 cm × 7. Column temp.: 45°. Carrier: He, inlet pressure 0.8 atm.) II (1.50 g), I (1.50 g) and high boiling products (1.35 g) were obtained. Yield of II: 22% (based on the consumed I). II. ^{19}F-NMR (CCl_4) δ: -0.88, 2.15 (relative intensity 1: 1). ^{13}C-NMR ($(CD_3)_2CO$) δ: 118.76 (q. $J_{C-F}=271.5$ Hz), 122.96 (q. $J_{C-F}=273.0$ Hz). IR ($CHCl_3$) cm^{-1}: 1700 ($\nu_{C=C}$), 1340, 1150 (ν_{C-F}). Mass Spectrum *m/e*: 356 (M^+). High mass spectrum. Calcd. for C_8SF_{12}: 355.952. Found: 355.954.

b) In Gas Phase: I (58.5 g) was put in a 1 liter quartz tube connected to a cold trap; the system was evacuated and sealed. The bottom of the quartz tube was covered with aluminium foil to prevent liquid phase from irradiation. With the trap cooled at $-78°$, the tube was irradiated at 2537 Å for 72 hr. The oil in the trap was separated by trap-to-trap distillation *in vacuo*. II (13.7 g) was obtained. The higher boiling part in the trap and the oil in the quartz tube were combined and subjected to trap-to-trap distillation. I (34.8 g) was recovered and 5.0 g of high boiling product was obtained. Yield of II: 57.8% (based on the consumed I).

c) In Solution: The solution of I (1.0 g) in *n*-pentane (20 ml) was sealed in a quartz tube (ϕ 8 mm) *in vacuo* and irradiated with a low pressure mercury lamp for 12 hr. The ratio of II to I estimated from GLC was 1: 1.6. (Shimazu GC-3AF. Column: DEGS, ϕ 3 mm, l 3 m. Column temp.: 50°. Carrier: N_2, inlet pressure, 0.6 atm.) Many other small peaks were observed in GLC. GLC-mass spectrum of II: *m/e* 356 (M^+). Isolation of II by preparative GLC gave a small amount of pale yellow oil, in which traces of impurities were observed by GLC.

Dewar Thiophene Dimer (IV)——On addition of II (38 mg) to DMF (90 mg) crystals began to precipitate. The mixture was kept at room temperature for 20 hr. The precipitate was collected, washed with CH_3OH and sublimed *in vacuo*. Colorless prisms (IV), mp 121—122°, were obtained. Yield, 5.5 mg (14.5%). IR (KBr) cm^{-1}: 1727 ($\nu_{C=C}$), 1170 (ν_{C-F}). ^{19}F-NMR (CF_3COOH) δ: -1.63 (s), -0.63 (s) (relative intensity 1: 1). Mass Spectrum *m/e*: 712 (M^+), 388 ($C_8S_2F_{12}$). *Anal.* Calcd. for $C_{16}S_2F_{24}$: C, 26.97; F, 64.04; S, 8.99. Found: C, 27.16; F, 64.16; S, 8.93.

Treatment of II with dimethyl sulfoxide or triethylamine gave IV in 27% or 5% yield, respectively.

2,3,5,6-Tetrakis(trifluoromethyl)-4-thia-10-oxatetracyclo[5.2.1.0.^{2,6}0.^{3,5}]dec-8-ene (VIa)——Furan (Va) (32 mg) was added to a solution of 1,2,3,4-tetrakis(trifluoromethyl)-4-thiabicyclo[2.1.0]pent-2-ene (II) (41 mg) in $CHCl_3$ (0.2 ml) and the mixture was kept at room temperature for 30 min. After removal of $CHCl_3$ and excess V using a vacuum line, the residue was recrystallized from CH_3OH to give colorless needles (VIa) (24 mg, 49%), mp 132—133°. IR (KBr) cm^{-1}: 1173 (ν_{C-F}). ^{1}H-NMR (CCl_4) δ: 6.61 (2H, s, 8- and 9-H), 5.40 (2H, s, 1- and 7-H). ^{19}F-NMR (CCl_4) δ: -2.50 (s), -2.33 (s) (relative intensity 1: 1). Mass Spectrum *m/e*: 424 (M^+). *Anal.* Calcd. for $C_{12}H_4OSF_{12}$: C, 34.02; H, 1.15; S, 7.65; F, 53.17. Found: C, 33.96; H, 0.94; S, 7.55; F, 53.78.

1,7,8,9-Tetramethyl-2,3,5,6-tetrakis(trifluoromethyl)-4-thia-10-oxatetracyclo[5.2.1.0.^{2,6}0^{3,5}]dec-8-ene (VIb)——Tetramethylfuran (Vb) (33.2 mg) was added to the solution of II (96.1 mg) in $CHCl_3$ (0.25 ml). After the mixture was allowed to stand for 24 hr at room temperature, $CHCl_3$ was removed by using a vacuum line. The residue was recrystallized from CH_3OH to give colorless needles (VIb) (86 mg), mp 76°. IR (KBr) cm^{-1}: 1180 (ν_{C-F}). ^{1}H-NMR ($CDCl_3$) δ: 1.76 (6H, s, 1- and 7-CH_3), 1.77 (6H, s, 8- and 9-CH_3). ^{19}F-NMR ($CDCl_3$) δ: -6.92 (s), -4.28 (s), (relative intensity 1: 1). Mass Spectrum *m/e*: 461 (M$-$F), 356 (C_8SF_{12}), 124 ($C_8H_{12}O$). *Anal.* Calcd. for $C_{16}H_{12}OSF_{12}$: C, 40.00; H, 2.50; S, 6.67; F, 47.50. Found: C, 40.01; H, 2.68; S, 7.43; F, 46.80.

2,3,4,5-Tetrakis(trifluoromethyl)-9-oxatricyclo[4.2.1.0^{2,5}]-nona-3,7-diene (VIIa)——Triphenylphosphine (37 mg) was added to the solution of VIa (60 mg) in $CHCl_3$ (0.3 ml). After the mixture was allowed to stand for 1 hr at room temperature, it was separated using a vacuum line. Colorless oil (VIIa) (31 mg) was obtained. IR ($CHCl_3$) cm^{-1}: 1718 ($\nu_{C=C}$). ^{1}H-NMR ($CDCl_3$) δ: 6.63 (2H, s, 7- and 8-H), 4.89 (2H, s, 1- and 6-H). ^{19}F-NMR ($CDCl_3$) δ: -1.72 (s), 0.48 (s) (relative intensity 1: 1). GLC-Mass Spectrum *m/e*: 392 (M^+). High Mass Spectrum: Calcd. for $C_{12}H_4OF_{12}$: 392.007. Found: 392.009.

1,6,7,8-Tetramethyl-2,3,4,5-tetrakis(trifluoromethyl)-9-oxatricyclo[4.2.1.0^{2,5}]nona-3,7-diene (VIIb)——Triphenylphosphine (149 mg) was added to the solution of VIb (273 mg) in $CHCl_3$ (4 ml) and the mixture was kept at room temperature for 10 min. After removal of $CHCl_3$, the residue was purified by sublimation *in vacuo* to give colorless prisms (VIIb) (248 mg), mp 66°. IR (KBr) cm^{-1}: 1714 ($\nu_{C=C}$), 1180 (ν_{C-F}). ^{1}H-NMR ($CDCl_3$) δ: 1.75 (6H, s, 7- and 8-CH_3), 1.57 (6H, s, 1- and 6-CH_3). ^{19}F-NMR ($CDCl_3$) δ: -2.16 (s), -0.72 (s), (relative intensity 1: 1). Mass Spectrum *m/e*: 448 (M^+), 429 (M$-$F), 379 (M$-CF_3$), 124 ($C_8H_{12}O$). High Mass Spectrum: Calcd. for $C_{16}H_{12}OF_{12}$: 448.070. Found: 448.073.

2,3,4,5-Tetrakis(trifluoromethyl)-9-oxapentacyclo[4.2.1.0.^{2,5}0.^{3,8}0.^{4,7}]nonane (VIIIa)——II (114 mg) and Va (70 mg) were caused to react in *n*-pentane (0.2 ml) for 30 min and *n*-pentane and excess Va were removed by vacuum line. The residue was dissolved in CH_3CN (2 ml) and treated with triphenylphosphine (84 mg) at room temperature for 1 hr. The volatile materials in the mixture were transferred in a quartz tube (ϕ 8 mm) *in vacuo*. The sealed quartz tube was irradiated at $-10°$ with a low pressure mercury lamp for 71 hr. After removal of CH_3CN *in vacuo*, the residue was sublimed *in vacuo* to give colorless prisms (VIIIa) (7.8 mg), mp 156—157°. IR (KBr) cm^{-1}: 1187 (ν_{C-F}). ^1H-NMR ($CDCl_3$) δ: 5.64 (2H, m, 1- and 6-H), 3.69 (2H, m, 7- and 8-H). ^{19}F-NMR ($CDCl_3$) δ: 3.75 (m), 7.60 (s) (relative intensity 1: 1). Mass Spectrum *m/e*: 392 (M^+), 204 ($C_6H_2OF_6$), 188 ($C_6H_2F_6$), 68 (C_4H_4O). High Mass Spectrum: Calcd. for $C_{12}H_4OF_{12}$: 392.003. Found: 392.006.

1,6,7,8-Tetramethyl-2,3,4,5-tetrakis(trifluoromethyl)-9-oxapentacyclo[4.2.1.0.^{2,5}0.^{3,8}0.^{4,7}]nonane (VIIIb)—A solution of VIIb (150 mg) in CH_3CN (2 ml) was sealed in a quartz tube (ϕ 8 mm) with exclusion of air and irradiated at 40° for 60 hr with a low pressure mercury lamp. Acetonitrile was removed *in vacuo* and the residue was purified through a SiO_2-column in *n*-pentane solution. The effluent was recrystallized from CH_3OH to give colorless prisms (VIIIb) (22.6 mg), mp 205°. IR (KBr) cm^{-1}: 1173 (ν_{C-F}). ^1H-NMR (($CDCl_3$) δ: 1.63 (6H, m, 1- and 8-CH_3), 1.21 (6H, m, 6- and 7-CH_3). ^{19}F-NMR ($CDCl_3$) δ: 0.0 (s), 3.44 (s) (relative intensity 1: 1). Mass Spectrum *m/e*: 448 (M^+), 232 ($C_8F_{12}O^+$), High Mass Spectrum: Calcd. for $C_{16}H_{12}OF_{12}$: 448.070. Found: 448.069.

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