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FLUORO-KETONES IX. HYDRATION OF PERFLUOROALKYLPOLYKETONES AND THEIR REACTIONS FORMING NOVEL CYCLIC COMPOUNDS

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SUMMARY

The reactions between fluoro di- and tetraketones with water yield dihydroxy compounds, some of which react via hydrogen bonding with electron donating compounds e.g. water, ethanol, tetrahydrofuran and pyridine to form novel heterocyclic compounds. On thermolysis these cyclic compounds revert to the original ketones.

INTRODUCTION

The electronic effect of a CF_3 group on rendering an adjacent carbonyl more electrophilic has been well documented [1,2,3]. The increased electrophilic nature of the carbonyl group renders it more reactive to a variety of nucleophilic reagents. Water and ethanol have been reported to form isolable hydrates and hemiketals respectively. The stability of these resulting products appears to be a function of the type of fluorinated ketone. Hexafluoroacetone for example forms a series of hydrates, the monohydrate being a solid while the polyhydrates are liquids. We have recently reported the synthesis of some fluorine containing di- and tetraketones [4] where in the course of preparing these compounds we have isolated some additional products containing water, ethanol and tetrahydrofuran. These polyketones unlike simple monoketones offer the possibility of

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forming cyclic compounds due to their geometric structure. We are now reporting our further studies on the reactions of these fluoropolyketones with electron donating molecules and their cyclization to new heterocyclic structures.

RESULTS AND DISCUSSION

In our earlier studies [4] we have shown that some of the fluoro di- and tetraketones form addition products with H_2O, C_2H_5OH and C_4H_8O (THF, tetrahydrofuran). One of these compounds described as a complex $C_6H_5CCl_2C(O)(CF_2)_3C(O)CCl_2C_6H_5 \cdot H_2O \cdot THF$ (I) has now been isolated and characterized. In addition we have extended our study to other fluoropolyketones.

In the synthesis of $C_6H_5CCl_2C(O)(CF_2)_3C(O)CCl_2C_6H_5$, (II) the product actually isolated was the complex I. On heating in a vacuum, the H_2O and THF were eliminated to yield the free diketone. Elemental analysis of I indicated a 1:1:1 ratio of the diketone:H_2O:THF. Single crystal X-ray analysis revealed the structure as III (see Fig. 1).

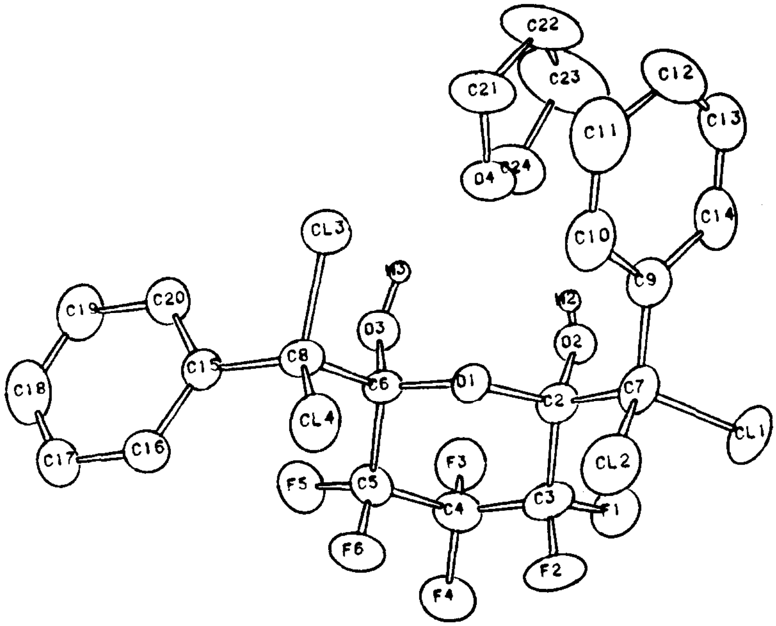
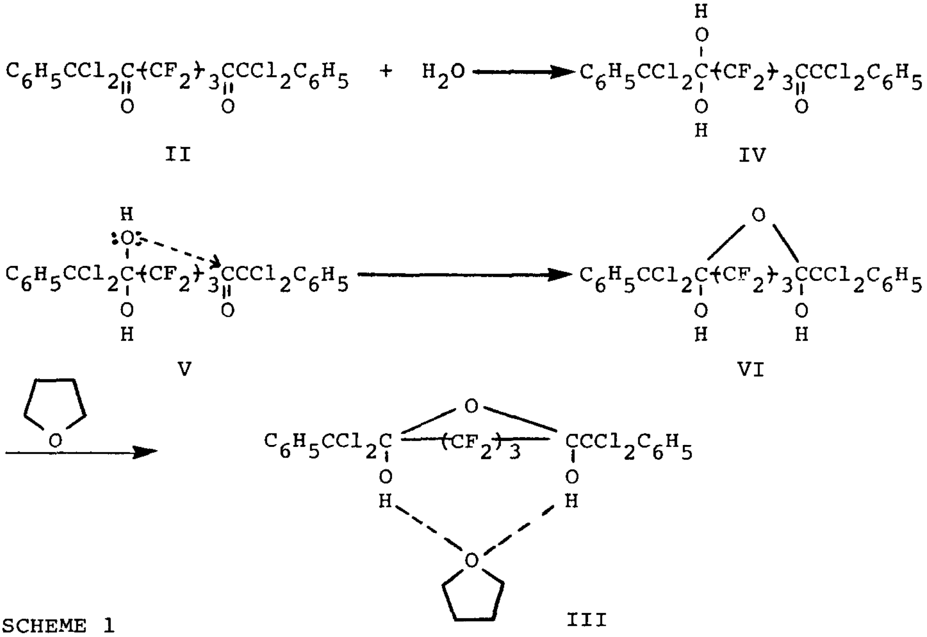


Fig. 1. Ortep Drawing of Compound III.

Since III could be thermally decomposed to the free diketone, thermal gravimetric analyses (TGA) were performed on the various complexes. The TGA of III indicated a loss of one molecule of THF followed by one molecule of H_2O. Mass spectral analysis showed a weak parent ion peak (M^+) and a significant $(M-H_2O-THF)^+$ fragment peak. Formation of this cyclic compound III, during the course of the synthesis (diethyl ether/THF solvent media followed by H_2O hydrolysis of the reaction mixture) is consistent with the following speculative reaction sequence shown in Scheme 1.



SCHEME 1

A molecular model of VI showed that the two OH groups are in the proper geometric configuration (OH groups are cis) to coordinate with a molecule of THF. In the absence of THF, the diketone can add two molecules of H_2O to produce compound VII. A TGA of VII indicated loss of two molecules of water and the regeneration of the free diketone. An X-ray analysis of VII showed the same molecular structure as for the THF adduct except for a molecule of H_2O replacing the THF (see Fig. 2).

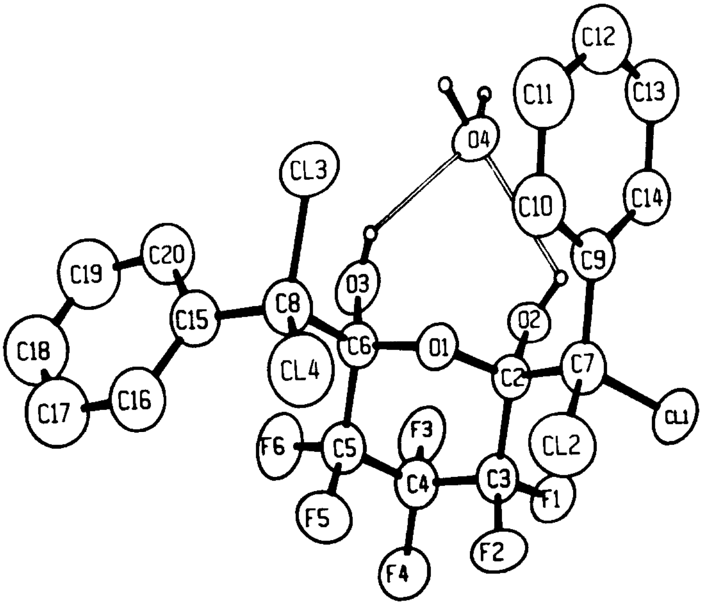


Fig. 2. Ortep Drawing of Compound VII.

Addition of THF to VII replaces one molecule of H_2O by a THF molecule to yield the complex III. The oxygen atom of THF is a better electron donor than H_2O (more basic) and forms a more stable hydrogen bond e.g. OH---O<

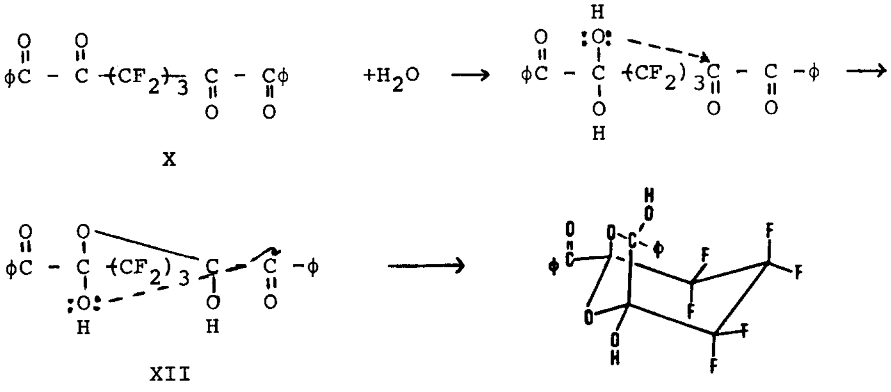
It has previously been shown [2] that THF can form complexes with fluorinated alcohols e.g. $H(CF_3)_2COH$---THF which in some cases were very stable and distillable liquids. Addition of C_2H_5OH containing 5% of water to the free diketone II formed a product VIII containing one molecule of H_2O and one molecule of C_2H_5OH. This product was sufficiently stable for a few days at room temperature allowing for characterization by infrared, ^1H NMR, elemental analysis and TGA. On standing under atmospheric conditions for a few weeks however the compound slowly decomposed by loss of C_2H_5OH and subsequent hydration by atmospheric moisture converting to VII. Apparently the hydrogen bonding between the two OH groups (in VI) and a molecule of C_2H_5OH is not as stable as with other molecules e.g. HOH or THF.

Other electron donating molecules capable of forming hydrogen bonds were examined. Dioxane, containing a small amount of water, which might form a bis complex since it has two oxygen atoms, reacted with the free diketone II to form a complex. The complex was too unstable to be isolated and characterized. Pyridine, containing a small amount of water, also formed a complex (IX) with the diketone II (see Table 2). The compound is sufficiently stable in the solid state to be characterized by elemental analysis, TGA and IR (in nujol only). The compound is unstable in solutions of diethyl ether, hexane or $CDCl_3$, reverting to the orginal ketone II. Because of this instability, it was not possible by solution IR and NMR to confirm the structure as IX.

If a longer chain perfluoroalkylether group e.g. $(CF_2)_4O(CF_2)_4O(CF_2)_4-$ or $-(CF_2)_4-$ is used in place of the $(CF_2)_3$ group, cyclic compounds were not formed on hydration of the diketone [4,5]. This would indicate that a $(CF_2)_3$ between two carbonyl groups is required for the formation of a more thermodynamically stable six member heterocyclic ring system.

The tetraketone $C_6H_5C(O)C(O)(CF_2)_3C(O)C(O)C_6H_5$ (X) [4] also forms cyclic compounds with H_2O or C_2H_5OH. Analysis of the compounds revealed a different cyclic structure. The two additional carbonyl groups (alpha to the C_6H_5) provide alternate reaction sites for the OH groups.

A reasonable mode of the cyclization reactions is shown in Scheme 2.



SCHEME 2

Analysis of compound XIII (see Table 2) as well as an X-ray characterization (see Fig. 3) confirms the structure as a bicyclic system. Unlike in compound VI, a molecular model of XIII shows that the two OH groups are not in proper geometric configuration to coordinate with electron donating molecules e.g. THF (see Fig. 3). For this reason only one molecule of H_2O or C_2H_5OH (XIV) reacts with the tetraketone.

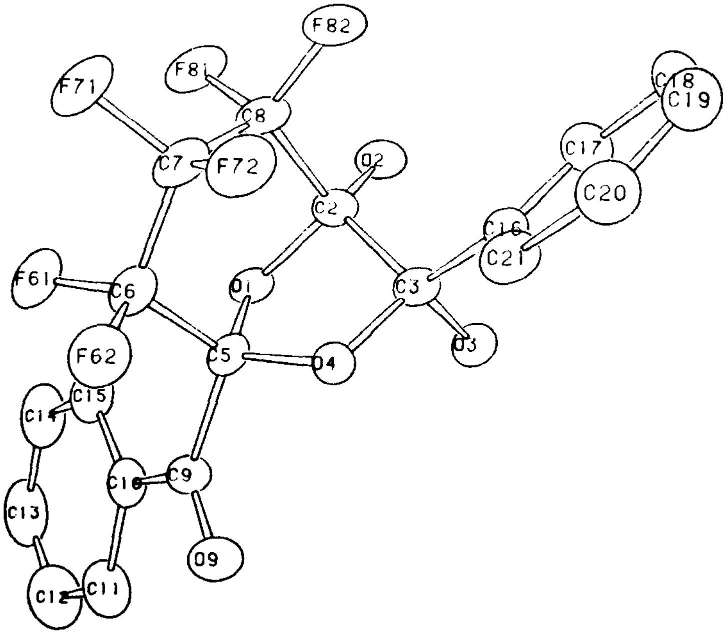


Fig. 3. Ortep Drawing of Compound XIII.

Attempts to form a cyclic compound with the diketone $C_6H_5C(O)(CF_2)_3C(O)C_6H_5$ (XV) [6] were also made. Unlike the ketones II and X, XV does not form a compound of comparable stability. Analysis of the reaction product of XV with H_2O indicated a 1:1 mole ratio compound. In the solid state this complex compound XVI is sufficiently stable to be analyzed by mass spectral, TGA and elemental analysis. The infrared analysis in nujol indicated the absence of a carbonyl band and the presence of the OH band. On standing for about one hour at room temperature the carbonyl band began to increase indicating decomposition of the cyclic compound (in nujol) to the diketone. Infrared analysis of XVI in $CDCl_3$, however, gave a spectrum equivalent to the diketone indicating the instability of XVI in solution. No ^1H NMR or ^{19}F NMR could be obtained since in solution the compound decomposed to the original diketone XV. Attempts at obtaining a crystalline sample for X-ray analysis were unsuccessful. The structure as shown in Table 2 is therefore tentative.

From the above studies it may be concluded that certain factors are required to form stable cyclic compounds. A six member cyclic compound resulting from the presence of a $-(O)C(CF_2)_3C(O)-$ group is required. The $\text{-(}CF_2\text{)-}_3$ group increases the electrophilic character of the carbonyl groups. If an additional electron withdrawing group is adjacent to the carbonyl group e.g. ϕCCl_2 or $\phi C(O)$, the electrophilic character of the $(O)C(CF_2)_3$ may increase further. The effect may be seen by examining the carbonyl stretching frequencies [6,7] of the following ketones (Table 1). From our studies and earlier reports it appears that the more electrophilic carbonyl group forms more stable compounds with H_2O to yield the hydroxy derivatives. Previous investigators have prepared stable hydrates of a number of fluorine containing ketones [2]. Similarly alcohols have been reacted with fluoroketones to form hemiketals [9].

TABLE 1

C=O Stretching Vibrations

	cm^{-1} (liquid phase)
$C_6H_5C(O)(CF_2)_3C(O)C_6H_5$	1710
$C_6H_5CCl_2C(O)(CF_2)_3C(O)Cl_2CC_6H_5$	1760
$C_6H_5C(O)\overset{*}{C}(O)(CF_2)_3\overset{*}{C}(O)C(O)C_6H_5$	1750
$C_8F_{17}C(O)\overset{*}{C}(O)CF_2CF_2OCF(CF_3)_2$	1757
$C_8F_{17}C(O)CF_2CF_2OCF(CF_3)_2$	1790
$CF_3C(O)CF_3$	1807 (gas phase) [8]

The bis hydroxy compounds of our study can subsequently react with electron donating molecules to form cyclic derivatives via hydrogen bonding.

EXPERIMENTAL

General Comments

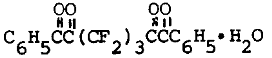
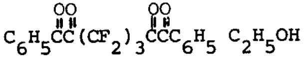
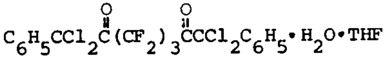
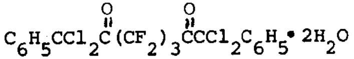
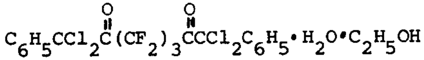
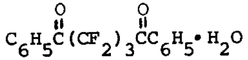
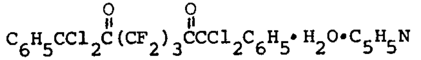
The starting materials $C_6H_5C(O)(CF_2)_3C(O)C_6H_5$, $C_6H_5CCl_2C(O)(CF_2)_3C(O)CCl_2C_6H_5$ and $C_6H_5C(O)C(O)(CF_2)_3C(O)C(O)C_6H_5$ were synthesized by procedures previously reported [4,6,7]. Most compounds were characterized by a combination of analytical techniques e.g. TGA, IR, NMR, GC/MS, combustion and X-ray analyses. Mass spectral analysis were carried out on a duPont model 21-490 mass spectrometer using chemical ionization mode. NMR spectra were performed on a XL-100-15 spectrometer using $CDCl_3$ solvent and TMS and $CFCl_3$ as internal references for ^1H and ^{19}F respectively. Analyses of the various reaction products are summarized in Tables 2 and 3.

X-ray Crystallographic Analysis

Colorless crystals of III and XIII, both shaped as rectangular parallelepipeds and colorless plate-like crystals of VII were grown by recrystallization from a diethyl ether/petroleum ether (30-60°C) (1:1 volume) solution. Crystalytics Company, Lincoln, Nebraska, furnished the experimental X-ray intensities and the following crystal data for III and XIII, whereas the X-ray facility at the University of Arizona supplied the complete structure solution and crystal data for VII: (III) - space group $P2_12_12_1$; $\underline{a}$ = 9.331(3)Å; $\underline{b}$ = 15.800(5)Å; $\underline{c}$ = 17.376(5)Å; Z=4; μ(MoKα) = 5.4 cm^{-1}; D_{calc} = 1.60 g cm^{-3}; (XIII) - space group $P2_1/n$; $\underline{a}$ = 6.803(3)Å; $\underline{b}$ = 23.574(7)Å; $\underline{c}$ = 11.481(5)Å; β = 98.77(3)°; Z=4; (MoKα) = 1.7 cm^{-1}; D_{calc} = 1.59 g cm^{-3}; and for (VII) - space group $P2_1/c$; $\underline{a}$ = 15.174(6)Å; $\underline{b}$ = 8.080(2)Å; $\underline{c}$ = 17.651(6)Å; β = 92.52(3)°; μ(MoKα) = 6.2 cm^{-1}; Z=4; D_{calc} = 1.73g cm^{-3}. A total intensity loss of 10.3% for III and 5.1% for VII was observed for the standard reflections. No significant loss was noted for XIII. The ω-scan method was used to collect 3935($2\theta_{max}$ = 59°) and 4179 ($2\theta_{max}$ = 55°) unique reflections for III and XIII,

TABLE 2

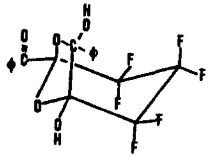
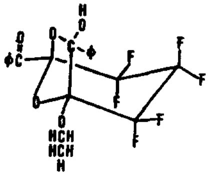
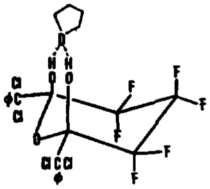
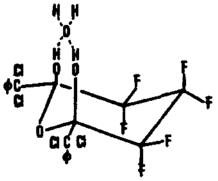
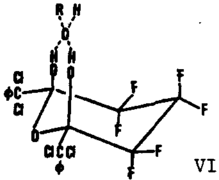
Characterization of Compounds[c]

Compound	Dec. Point °C	TGA % calc'd/ found	1R[a], cm^{-1} C = O	OH	M.S.
 $C_6H_5\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}(CF_2)_3\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}C_6H_5\cdot H_2O$ (XIII)[b]	128-135	4.1/4.0	1660 (vs) 1690 (sh)	3360 (vs,br)	$434,(M)^+$ $416,(M-H_2O)^+$
 $C_6H_5\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}(CF_2)_3\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}C_6H_5\ C_2H_5OH$ (XIV)(nc)	103-110	10.0/9.0	1689 (s) 1660 (s)	3340 (s,br)	$462,(M)^+$ $416,(M-C_2H_5OH)^+$
 $C_6H_5CCl_2\overset{O}{\overset{\|}{C}}(CF_2)_3\overset{O}{\overset{\|}{C}}CCl_2C_6H_5\cdot H_2O\cdot THF$ (III)[b]	99-115	-THF 11.7/11.1 $-H_2O$ 2.9/3.0	-	3240 (vs,br)	$614,616,618,(M)^+$ 524,526,528 $(M-H_2O-THF)^+$
 $C_6H_5CCl_2\overset{O}{\overset{\|}{C}}(CF_2)_3\overset{O}{\overset{\|}{C}}CCl_2C_6H_5\cdot 2H_2O$ (VII)(nc)	85-110	6.4/6.5	-	3602 (s) 3520 (m) 3380 (s,br) 3240 (m,br)	524,526,528 $(M-2H_2O)^+$
 $C_6H_5CCl_2\overset{O}{\overset{\|}{C}}(CF_2)_3\overset{O}{\overset{\|}{C}}CCl_2C_6H_5\cdot H_2O\cdot C_2H_5OH$ (VIII) (nc)	90-110	$-C_2H_5OH$ 7.8/7.7 $-H_2O$ 3.1/4.0	-	3602 (s) 3528 (s) 3300 (vs,br)	524,526, 528 $(M-H_2O-C_2H_5OH)^+$
 $C_6H_5\overset{O}{\overset{\|}{C}}(CF_2)_3\overset{O}{\overset{\|}{C}}C_6H_5\cdot H_2O$ (XVI)(nc)	85-93	4.8/5.5	-	3420 3320	$378,(M)^+$ $360,(M-H_2O)^+$
 $C_6H_5CCl_2\overset{O}{\overset{\|}{C}}(CF_2)_3\overset{O}{\overset{\|}{C}}CCl_2C_6H_5\cdot H_2O\cdot C_5H_5N$ (IX)(nc)	62-85	15.6/15.2 $(-H_2O + C_5H_5N)$	-	3340	524,526,528 $(M-H_2O-C_5H_5N)^+$

[a] Determined as KBr pellet except for compounds XVI and IX which were in Nujol mull.
[b] Reported previously in Ref. 4.
[c] All new compounds had correct C,H and Cl analyses.

TABLE 3

^{1}H NMR and ^{19}F NMR Data (in $CDCl_3$ solvent)

Compound	^{19}F ($CFCl_3$ ref., ppm)	^{1}H (TMS ref., ppm)
 XIII	-113.4, -134.2 (AB pattern, -118.0, -130.2 each a mult.) -119.8, -139.2 " " -120.2, -130.2 " " -125.6, -127.2 " "	8.28 (mult., 3 ar. H) 7.53 (mult., 7 ar. H) 5.88 (very broad, O-H)
 XIV	-118.9 (half of AB pattern, -121.1 doub.) " -121.5 " " -127.0 (other half of AB -130.0 pattern, doub.) -139.9 " "	8.3-8.5 (mult., 4 ar. H) 7.4-7.7 (mult., 6 ar. HO) 6.06 (sing., 1H, OH) 4.04[a] (pent., by 7.5 Hz, 1H, CH_2) 3.37[a] (pent., by 7.5 Hz, 1H, CH_2) 1.23 (trip., by 7.0 Hz, 3H, CH_3)
 III	-118.5 (doub. by 272 Hz) -123.8 (AB pattern) -140.6 (doub. by 272 Hz)	8.0, 7.4 (mult., 10 ar. H) 5.8 (broad sing., 2H,OH) 3.66, 1.84 (pent., 8H, THF)
 VII	-118.6 (doub. by 272 Hz) -123.8 (AB pattern) -140.6 (doub. by 272 Hz)	8.0, 7.4 (mult., 10 ar. H) 5.0 (broad sing., 2H, OH) 1.7 (broad sing., 2H, H_2O)
 VIII	—	8.0, 7.4 (mult., 10 ar. H) 3.7 (broad sing. and quart. 5H, OH and CH_2) 1.2 (trip., 3H, CH_3)

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[a] Two $-CH_2$ environments indicate the possibility of 2 isomers where OH and OC_2H_5 may be interchanged.

respectively. The corresponding value for VII is 2847($2\theta_{max}$ = 45^o) collected using the θ-2θ scan mode. The structures were solved by direct methods and refined to a final R-index of 0.051, 0.072, and 0.068 for III, XIII and VII, respectively.

The asymmetric unit of III contains one THF molecule which is bound to (VI) by two nearly symmetric hydrogen bonds. The 04---02 and 04---03 contacts are 2.732(4)Å and 2.707(4)Å, respectively. Similarly, in VII, each asymmetric unit contains one water molecule which is also bound to VI by two hydrogen bonds. The hydrogen bond contacts are 2.713Å for 04---02 and 2.884Å for 04---03.

Synthesis of XIII

To a diethyl ether (5 ml) solution of $C_6H_5C(O)C(O)(CF_2)_3C(O)C(O)C_6H_5$ (X) (2.0g, 4.81 mmol) at 25°C was added water (0.2 ml). The solution was stirred for 2 h and subsequently dried ($MgSO_4$). The solvent was removed in a current of air at room temperature. The crude solid product was washed with hexane (3 x 5 ml) to yield 1.96g (94%) of white crystals. Recrystallization from diethyl ether and petroleum ether (30-60°C) (1:1 volume ratio) yielded single crystals for the X-ray analysis.

When the above reaction was repeated in the presence of tetrahydrofuran instead of diethyl ether, the same product XIII was obtained.

Synthesis of XIV

The reaction was carried out in flame dried glassware under an atmosphere of purified dry nitrogen. Anhydrous C_2H_5OH (5 ml) was added to $C_6H_5C(O)C(O)(CF_2)_3C(O)C(O)C_6H_5$ (2.0g, 4.81 mmol) and stirred for 1 h. The solvent was removed in a stream of dry nitrogen. The crude product was washed with petroleum ether (30-60°C, 5 x 2 ml) to yield 2.05g (92%) of XIV compound.

Synthesis of Compounds III, VII and VIII

To a tetrahydrofuran (5 ml, for compound III), diethyl ether (5 ml, for compound VII) or 95% C_2H_5OH-5% H_2O (5 ml, for compound VIII) solution of $C_6H_5CCl_2C(O)(CF_2)_3C(O)CCl_2C_6H_5$ (II) (2.0g, 3.80

mmol) at 25°C was added water (0.2 ml, none for reaction with 95% C_2H_5OH-5% H_2O). The reactions were stirred for 3 h and dried ($MgSO_4$). The solvents were removed in a current of air at room temperature. The crude products were washed with petroleum ether (30-60°C, 4 x 2 ml) to yield the compounds III, 2.23g (95%); VII, 2.02g (94%) and VIII 1.95g (90%) respectively. Recrystallization from diethyl ether and petroleum ether (30-60°C) (1:1 volume ratio) yielded single crystals for X-ray analyses.

Synthesis of Compound XVI

A solution of $C_6H_5C(O)(CF_2)_3C(O)C_6H_5$ (XV) (1g, 2.78 mmol) in diethyl ether (2 ml) was stirred with water (0.2 ml) for 20 h at 25°C. The solution was dried ($MgSO_4$) and the solvent was removed by passing a current of air at room temperature. The crude residue was washed with hexane (5 x 2 ml) yielding a white crystalline product, 0.85g (81%). On standing at room temperature, compound XVI changed to the starting diketone. At lower temperature ∿ 0°, XVI was stable for over a month.

Synthesis of Compound IX

To a pyridine (5 ml) solution of $C_6H_5CCl_2C(O)(CF_2)_3C(O)$-$CCl_2C_6H_5$ (1.0g, 1.90 mmol) at 25°C was added water (0.5 ml). The solution was stirred for 20 h and subsequently dried ($MgSO_4$). The solvent was removed in a current of air at room temperature. The resulting liquid was washed with hexane (4 x 5 ml). The liquid residue was placed in a desiccator and dried under vacuum for 2 h. The resulting crude solid was again washed with hexane (3 x 2 ml) and dried to yield 0.80g (68%) of a white solid product IX. Attempts to recrystallize the compound from diethyl ether/petroleum ether solvents was unsuccessful since the compound decomposed, reacted with atmospheric or solvent water and reverted to VII.

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