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THE CYCLOADDUCTS OF HEXAFLUOROACETONE AND -THIOACETONE WITH DIPHENYLKETENE

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SUMMARY

Hexafluoroacetone reacted with diphenylketene in the presence of potassium fluoride to give a 1:1 cycloadduct of β-lactone structure. On the other hand, hexafluorothioacetone, liberated from 2,2,4,4-tetrakis(trifluoromethyl)-1,3-dithietane by potassium fluoride, reacted with diphenylketene to give a "reverse" cycloadduct, a 3-thietanone derivative. Several reactions of the above products, including a reductive desulfuration of the 3-thietanone derivative were carried out.

INTRODUCTION

Hexafluoroacetone is known to be an active reaction partner in numerous reactions [1]. Cycloadditions have been reported with compounds containing an isolated double bond, as e.g. vinyl ethers [2, 3], with compounds containing a triple bond, as e.g. alkoxyacetylene [4]. In addition, there have been reported a few examples for the cycloadditions of hexafluoroacetone [5] and its less fluorinated analogues [6, 7] with unsubstituted ketene.

We wish to report here, on the cycloadditions of hexafluoroacetone and hexafluorothioacetone with diphenylketene.

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RESULTS AND DISCUSSION

The cycloadduct of hexafluoroacetone with diphenylketene

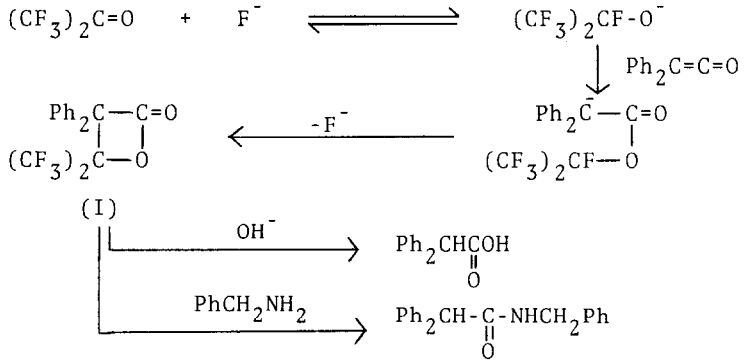
While 1,3-difluoro- and 1,1,1-trifluoroacetone require catalysts, e.g. $ZnCl_2$, to react with ketene and form the expected β-lactones [6, 7], hexafluoroacetone is reported to react with ketene in the absence of any catalyst at -78°C to give the lactone of β,β-bis(trifluoromethyl)-β-hydroxypropionic acid in quantitative yield [5].

In contrast to this easy reaction of unsubstituted ketene, diphenylketene did not react with hexafluoroacetone, even at prolonged heating at 100°C. Then, we carried out the reaction not with hexafluoroacetone itself, but with its complex formed with potassium fluoride, in a polar aprotic solvent, as acetonitrile or dimethylformamide:

$$(CF_3)_2C{=}O \quad + \quad KF \rightleftharpoons (CF_3)_2CF\text{-}O^-K^+.$$

This complex is known to be reactive enough in various reactions, [8, 9, 10], though no cycloaddition has been reported, as yet.

In the present work, the complex was prepared in situ according to the method of Evans and co-workers [8], and then equimolar amount of freshly prepared diphenylketene was added at room temperature. A slightly exothermic reaction occurred, and the product could be isolated by fractional distillation in a yield of 59%. Elementary analysis suggested a 1:1 adduct, and based upon the various spectral data the β-lactone structure (I) was assigned to the product.

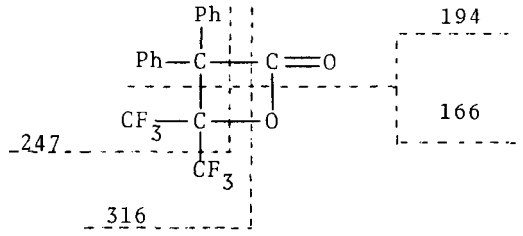


The IR spectrum showed a peak due to the lactone group at 1860 cm^{-1},

which corresponded to the absorption at 1850 cm^{-1} of the β-lacton dimer of diphenylketene [11]. The proton NMR showed only aromatic protons, while the fluorine NMR consisted of one singlet.

The magnetic equivalence of the two trifluoromethyl groups suggests that the four membered ring is nearly planar, and the two trifluoromethyl groups are located above and under this plane nearly symmetrically.

The mass spectrum confirmed the assumed structure. It gave a strong molecular peak (59%), which refers to the increased stability of the β-lactone ring due to the presence of the strongly electron attracting CF_3 groups, and contained a considerable peak at m/e 316, corresponding to the fragment M^+-CO_2. The base peak appeared at m/e 165, which can be attributed to a consecutive fragmentation of the diphenylketene fragment. The main directions of the fragmentation were as follows:



In order to obtain the cycloadduct as main product, it is essential that the reaction mixture does not contain free potassium fluoride, i.e., all the catalyst should be applied in the form of its complex with hexafluoroacetone. In an attempt to react the same reactants in the presence of excess potassium fluoride, besides a small amount of impure cycloadduct, a colorless solid was isolated in a yield of 41%, which was identified to be the β-lactone dimer of diphenylketene [11]. The formation of the dimer may be explained in that the basicity of potassium fluoride is sufficient to catalyze the dimerization of ketene in a polar solvent.

For further evidence of the structure of this cycloadduct (I), we investigated the hydrolysis of this compound, as follows.

The reaction conditions for the hydrolysis of β-lactones to the corresponding β-hydroxy acids differ markedly, depending upon the substituents of the saturated carbon atoms of the four

membered ring. For example, β,β-bis(trifluoromethyl)-propiolactone is reported to be hydrolyzed very easily at room temperature under either acidic, neutral or alkaline condition [5]. Attempting to hydrolyze (I), it was found to be very stable, when worked in heterogenous systems. For example, boiling (I) with 10% aqueous sodium hydroxide solution, the ring remained intact and a stable and volatile monohydrate of (I) was isolated. The anhydrous compound could be recovered by drying the hydrate at 120 - 130°C/ 20 - 25 mmHg for three hours. For this reason, further hydrolysis attempts were carried out in a sealed tube.

While no reaction occurred by heating (I) with water or 95% sulfuric acid up to 150°C, alkaline hydrolysis with 10% aqueous sodium hydroxide at 150°C resulted in the loss of hexafluoroacetone, and diphenylacetic acid was isolated (yield 76%). In contrast to the above, hydrolysis in homogenous system, i.e., in methanolic sodium methoxide solution, proceeded under much milder conditions: during 72 hours at room temperature. The product in this case was also diphenylacetic acid (92%). This striking difference between the rate of hydrolysis in homogenous and heterogenous systems suggests that the hydrophobic character of (I) is one of the reasons for the stability of the cycloadduct under hydrolysis conditions.

Thus the expected β-hydroxy acid, $(CF_3)_2\underset{\underset{OH}{|}}{C}\text{-}C(Ph)_2CO_2H$, could not be isolated by the hydrolysis of (I). This may be ascribed to low stability of the acid, which presumably decomposed into stable hexafluoroacetone hydrate and diphenylacetic acid.

Analogously to the hydrolysis, reaction of (I) with benzylamine did not lead to the expected β-hydroxy amide, but to N-benzyldiphenylacetamide instead.

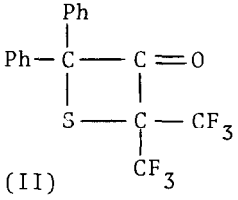
The cycloadduct of hexafluorothioacetone with diphenylketene

The cycloadditions of hexafluorothioacetone with isolated and conjugated C=C double bond systems have been reported [4], resulting in the formation of 1,2- and 1,4-cycloadducts, respectively. Recent works in our laboratory [12] extended these cycloadditions to some other isolated C=C double bond systems, and showed, that instead of the inconvenient hexa-

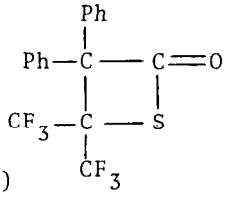
fluorothioacetone (b.p. 8°C), its stable dimer 2,2,4,4-tetrakis-(trifluoromethyl)-1,3-dithietane (b.p. 110°C) can be used, the monomer being liberated from this upon the effect of potassium fluoride in aprotic solvents.

No reactions of fluorinated thioketones with cumulated double bond systems have been reported as yet. In the course of our studies, hexafluorothioacetone was always generated in situ from its dimer, which can be prepared from hexafluoropropene and sulfur directly [13], by means of potassium fluoride.

Thus, diphenylketene reacted with equimolar amount of the dimer in the presence of potassium fluoride, i.e. two equivalents of the monomer, in polar aprotic solvents, as dimethylformamide, sulfolane, and acetonitrile, at temperatures between -30 - +60°C, to yield a pale yellow liquid. Although the yield and purity varied remarkably with the reaction conditions, the best method was found to consist of reacting equimolar amounts of the reactants in dimethylformamide at room temperature. Thus the product could be obtained in a yield of 59%. The structure (II) was assigned based upon the following data.



(II)



(III)

Elementary analysis showed a 1:1 adduct, (II) or (III). The characteristic bands in the IR spectrum were at 1795 cm^{-1} (C=O, the analogous cyclobutanones generally absorb at 1787 cm^{-1} [14]) and 1140 - 1320 cm^{-1} (C-F). Proton NMR showed only aromatic protons, and fluorine NMR revealed a singlet peak.

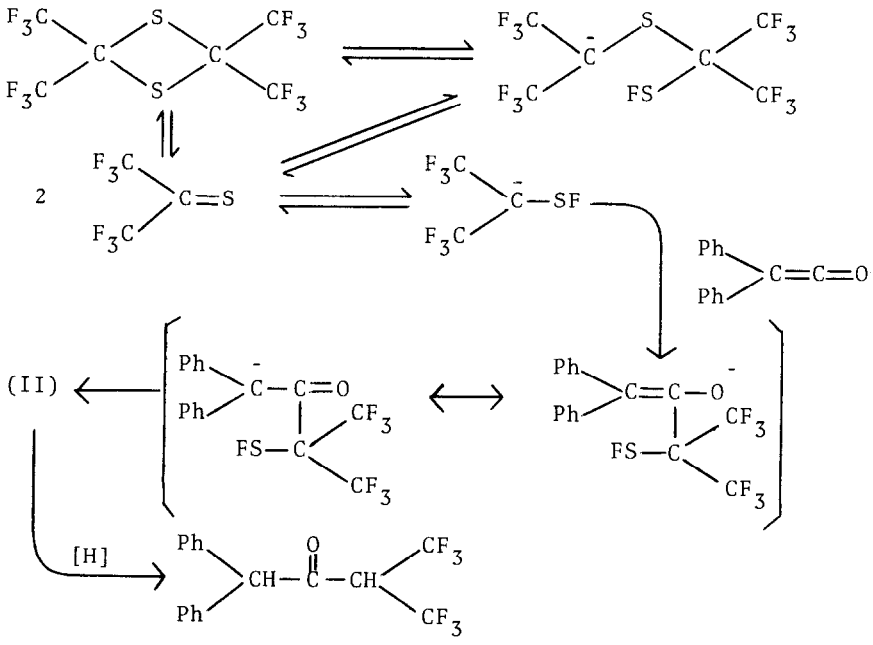
In the mass spectrum the molecular peak was of significantly lower intensity, than that of the cycloadduct of hexafluoroacetone and diphenylketene, suggesting a less stable ringsystem. The base peak appeared again at m/e = 165, originating in the fragmentation of the diphenylketene fragment. The second strongest peak was at m/e = 198 (54%), corresponding to the mass of thiobenzophenone, affording thus evidence of the suggested structure (II). Furthermore, in the case of the structure

(III), analogous to the cycloadduct (I), splitting off of COS could be expected, and consequently M^+ - COS = 310 should be observed. No peak was actually observed at m/e 310.

The formation of the cycloadduct (II), rather than of (III) should be "reversely" oriented cycloaddition, in order to emphasize the difference between this and the "normal" cyclo-addition of the oxygen analogue, (I).

To explain the formation of (II), there must be assumed, that in the transition state the sulfur atom becomes partially positive. A few examples have been reported, when thioketones, polarized in the way $\rangle C^{\delta-}=S^{\delta+}$, reacted differently from oxygen containing analogues [15, 16, 17].

This behaviour, as was pointed out by Opitz [15], can well be explained by the differences in the polarizability, size and electronegativity of the heteroatoms in $\rangle C{=}O$ and $\rangle C{=}S$ systems. With its relatively strong (2p-2p)π bond, the carbonyl group is strongly polar, but difficult to polarize, where as thiocarbonyl group with its more diffuse (2p-3p)π bond is weakly polar, but easily polarizable. For the mechanism of this cycloaddition, the following way may be suggested.



Hydrolysis in neutral and acidic medium up to a temperature of 150°C left the compound intact. Alkaline hydrolysis with 10% aqueous sodium hydroxide at 170°C resulted in a very complex reaction mixture, while at 150°C conversion was only partial. Alkaline hydrolysis in homogenous system (methanolic sodium methoxide) proceeded smoothly at room temperature within 72 hours. However, it led to a mixture of several decomposition products.

Reduction of the cycloadduct (II) with lithium aluminum hydride at -5 - 0°C in tetrahydrofuran led to a solid in a yield of 41%. The structure of this compound was established from its spectral data, as to be diphenylmethyl bis(trifluoromethyl)-methyl ketone. The reduction affords an additional proof for the structure (II).

Reductive desulfurations of sulfides and thietanes have been reported to occur upon the effect of Raney nickel in an inert solvent, generally at elevated temperature [18, 19]. The reduction of the 3-thietanone (II) with lithium aluminum hydride at low temperature presented above is a new way of reductive desulfuration of four membered, S-containing ring, and may probably be well utilized in the case of compounds, sensitive for heating.

EXPERIMENTAL

Diphenylketene

Diphenylketene has been prepared in several ways, of which the following two are of practical use: (a) dehydrohalogenation of diphenylacetyl chloride [20], and (b) thermal decomposition of azibenzil, followed by spontaneous rearrangement of the formed carbene [21]. While the latter route has been extensively used in the literature, the former, described first by Staudinger [20], is much simpler. Though Staudinger did not isolate diphenylketene in substantia, we found that a modified procedure described below provides an appropriate way to prepare diphenylketene on a scale of about 10 g per batch. In a 300 ml round bottomed flask, equipped with mechanical stirrer, reflux condenser with $CaCl_2$ tube, dropping funnel, and gas inlet tube, diphenylacetyl chloride (23.1 g, 0.1 mole) was dissolved in dry ether (150 ml) at room temperature, under dry nitrogen. After com-

plete dissolution dried triethylamine (13.9 ml, 10.1 g, 0.1 mole) diluted with dry ether (30 ml) was added dropwise in an interval of about 20 minutes, with external water cooling in order to maintain room temperature, similarly in a nitrogen atmosphere. After the addition, the mixture was stirred for additional 30 minutes, and then the triethylamine salt was filtered and washed with dry ether rapidly. The filtrate was kept under nitrogen (constant bubbling in), until further work up. The solvent was removed as follows: a Claisen-flask was equipped with a gas inlet tube and a dropping funnel, and was heated to 55 - 60°C in an oil-bath. The ethereal solution of diphenylketene was introduced dropwise into the flask through the dropping funnel, while a rapid stream of dry nitrogen was led into the flask. Ether distilled instantaneously, and the crude diphenylketene remained in the flask. After evaporation of all the ether, the dropping funnel was exchanged for a thermometer and the gas inlet tube for a distillation capillary. Diphenylketene was distilled, similarly in an atmosphere of dry nitrogen, as reddish yellow liquid, b.p. 120 - 126°C/ 2 mmHg (lit. [21], b.p. 120°C/ 3.5 mmHg). Yields in several runs varied between 51.6 - 60.0% (10.1 - 11.6 g). The product contained only traces of diphenylketene oligomers, as was shown by the IR spectrum. The ketene was generally used immediately after preparation, but it could be stored under nitrogen at 0 - 5°C for a few days without any significant change.

4,4-Bis(trifluoromethyl)-3,3-diphenyloxetan-2-one (I)

Hexafluoroacetone was bubbled at a slow rate into a vigorously stirred suspension of freshly dried potassium fluoride (1.16 g, 20 mmole) in dry dimethylformamide (30 ml) at room temperature, until all the solid disappeared (about 30 minutes). Freshly prepared diphenylketene (3.9 g, 20 mmole) diluted with dry dimethylformamide (10 ml) was added dropwise at room temperature within 10 minutes. The color of the ketene disappeared instantaneously. The mixture was stirred for 3 hours and then allowed to stand overnight. The formed reddish-yellow solution was distilled directly. After removal of the solvent, the fraction boiling at 120 - 122°C/ 1 mmHg, a pale greenish oil was collected (4.95 g, 68.8%), which upon inoculation, soon crystallized.

The crystals were filtered and pressed down, whereupon a small amount of oil was removed. The product obtained in this manner (4.26 g, 59.3%, m.p. 55 - 60°C) was pure enough for further experiments. For analytical purpose a sample was recrystallized from petroleum ether (b.p. 40 - 55°C), giving colorless plates, m.p. 63 - 65°C. Analysis: Found: C, 56.09; H, 3.24; F, 31.22%. $C_{17}H_{10}F_6O_2$ requires C, 56.8; H, 2.8; F, 31.6%. IR (KBr): 1861 (C=O), 1120 - 1350 (br, C-F) with peaks at 1150, 1210, 1255, 1290 and 1310 cm^{-1}. ^{19}F NMR (in CCl_4)**: δ -9.7 ppm (s, CF_3). ^1H NMR (in CCl_4): δ 7.2 - 7.6 ppm (m, ArH). MS: M^+ 360. Base peak: m/e 165. Main fragments: m/e 316 (18%) M-CO_2; m/e 247 (22%) M-CO_2-CF_3; m/e 194 (50%) diphenylketene; m/e 166 (44%) hexafluoroacetone. When acetonitrile was used as solvent, (I) could be obtained in a yield of 47.3%.

Alkaline hydrolysis of (I)

(a) In heterogeneous system

A mixture of (I) (20 g, 5.55 mmole) and 10% aqueous sodium hydroxide solution (30 ml) was heated and stirred in a sealed tube for 3 hours at 150 - 155°C, whereupon the insoluble starting material was dissolved. After cooling, the solution was filtered, acidified with conc. sulfuric acid, and extracted with chloroform. The extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness. Crude diphenylacetic acid (0.9 g, 76.3%, m.p. 130 - 142°C) thus obtained was recrystallized from cyclohexane giving the pure acid, m.p. 141 - 144°C. No depression of m.p. was observed upon admixture with an authentic sample. The structure was confirmed by IR spectrum as well.

(b) In homogeneous system

Metallic sodium (0.3 g, 15.2 mmole) was dissolved in methanol (30 ml) and this solution was combined with a solution of (I) (2.0 g, 5.55 mmole) in methanol (10 ml). The mixture was allowed to stand for 3 days at room temperature. After evaporation to dryness the solid residue was dissolved in water (30 ml), filtered, and acidified with 10% aqueous hydrochloric

** All the ^{19}F NMR chemical shifts throughout this article are given in δ ppm from external trifluoroacetic acid.

acid. The separated crystals were collected, washed with water and dried. Diphenylacetic acid (1.08 g, 91.6%, m.p. 142 - 144 ^{o}C) was thus obtained.

Reaction of (I) with benzylamine

A solution of (I) (1.0 g, 2.78 mmole) and benzylamine (0.30 g, 2.80 mmole) in acetonitrile (10 ml) was refluxed for 2 hours and then allowed to stand overnight. Evaporation to dryness gave a pale yellow oil (2.3 g) which crystallized upon standing giving a sticky solid. Crystallization from cyclohexane resulted in diphenylacetic acid N-benzylamide (0.6 g, 69.7%), melting at 120 - 126^{o}C. Recrystallization from isopropanol gave a pure sample, m.p. 124 - 126^{o}C. No depression of melting point upon admixture with an authentic sample was observed. By partial evaporation of the solvent from the original cyclohexane mother liquor gave a second crop (0.16 g, m.p. 118 - 124^{o}).

2,2-Diphenyl-4,4-bis(trifluoromethyl)thietan-3-one (II)

To a vigorously stirred mixture of potassium fluoride (3.65 g, 62.4 mmole), dry dimethylformamide (50 ml) and hexafluorothioacetone dimer (22.7 g, 62.4 mmole), freshly prepared diphenylketene (12.1 g, 62.4 mmole), diluted with dry dimethylformamide (20 ml), was added dropwise, during 15 minutes at room temperature. The color of the reaction mixture turned deep blue soon after starting the addition of the ketene. After stirring for 3 hours at room temperature, the mixture was allowed to stand overnight, then was poured into ice-water and extracted with ether. The ethereal extract was washed with water, dried over sodium sulfate and evaporated to dryness. The residual dark blue oil (18.4 g) was distilled in vacuo, and the fraction boiling at 120 - 123^{o}C/ 1 mmHg was collected. The thietane (II) was obtained in 59% yield (13.6 g). The freshly distilled product reveals a strong blue color which disappears within a few days upon standing. Analysis: Found: C, 54.74; H, 2.27; F, 30.96; S, 8.20%. $C_{17}H_{10}F_6SO$ requires C, 54.3; H, 2.69; F, 30.3; S, 8.53%. IR (film): 1795 (C=O), 1140 - 1320 (C-F) with peaks at 1150, 1200 and 1260 cm^{-1}. ^{19}F NMR (in CCl_4): δ -10.6 (s, CF_3). ^{1}H NMR (in CCl_4): δ 6.8 - 8.0 (m, Ar-H). MS: M^+ 376 (9%). Base peak: m/e 165. Main fragments: m/e

348 (17%) M-CO; m/e 279 (22%) M-CO-CF_3; m/e 198 (54%) thiobenzophenone; m/e 194 (5%) diphenylketene; m/e 182 (7%) hexafluorothioacetone.

Alkaline hydrolysis of the thietanone

A mixture of the thietanone (II) (8.0 g, 21.2 mmole) and 10% aqueous sodium hydroxide solution (40 ml) was heated with vigorous stirring in a sealed tube for 8 hours at 150 - 155°C. The reaction mixture consisted of a dark brown solution and some insoluble reddish-brown thick oil. The latter was removed by extraction with dichloromethane, and the aqueous solution was acidified with 10% hydrochloric acid giving crystals of diphenylacetic acid (0.26 g, 8.5%). By evaporation of the solvent from the dried dichloromethane extract, a dark colored oil (4.9 g) was obtained, distillation of which resulted in an almost colorless oil, b.p. 137 - 139°C/ 3 mmHg (2.7 g, 34.7%). The IR spectrum showed this to be somewhat impure unchanged (II).

Reduction of (II) with lithium aluminum hydride

The thietanone (II) (1.8 g, 4.8 mmole) dissolved in dry tetrahydrofuran (10 ml) was added dropwise during 10 minutes to a stirred suspension of lithium aluminum hydride (1.0 g, 26.4 mmole) in dry tetrahydrofuran (30 ml), kept at 0 - -5°C in an ice-salt bath. After the addition, stirring was continued at the same temperature for additional 30 minutes. The mixture was then poured into ice-water and acidified with 10% aqueous hydrochloric acid. The organic layer separated was extracted with ether, and dried over anhydrous sodium sulfate. Evaporation to dryness gave a dark yellow, thick oil (1.8 g), which on distillation yielded yellow oil (0.67 g, 40.0%), b.p. 127 - 129°C/ 2 mmHg, solidifying upon cooling. The distilled product was dissolved in petroleum ether, cooled to -78°C, and the separated crystals were collected and washed at this temperature, giving diphenylmethyl bis(trifluoromethyl)methyl ketone (0.44 g, 26.3%) as colorless crystals, m.p. 71 - 72°C. Analysis: Found: C, 58.60; H, 3.19; F, 33.0%. $C_{17}H_{12}F_6O$ requires C, 59.0; H, 3.4; F, 33.0%. IR (KBr): 1740 (C=O), 1120 - 1420 (C-F) with peaks at 1175, 1210, 1240, 1275, 1285, 1325 and 1370 cm^{-1}. ^{19}F NMR (in CCl_4): δ -15.5 (d, J_{F-H}= 7 Hz). ^1H NMR (in CCl_4):

δ 5.21 (s, $Ph_2C\underline{H}$), 4.11 [s, $(CF_3)_2C\underline{H}$, J_{H-F}= 7 Hz], 6.95 - 7.05 (m, ArH). MS: no parent peak. Base peak: m/e 167 (Ph_2CH^+). Additional peaks: m/e 179 [$(CF_3)_2CHC{=}O$], m/e 194 ($Ph_2C{=}C{=}O$), m/e 152 [$CH_2(CF_3)_2$].

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