Fluorinated β-Diketones in Reactions with Diazocyclopropane Generated in situ

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Treatment of 1,1-di- and 1,1,1-trifluoroalkane-2,4-diones **10**–**13** with cyclopropyldiazonium intermediates **2** and **3**, generated in situ through the decomposition of *N*-cyclopropyl-*N*-nitrosourea **1** by treatment with moist K_2CO_3, did not result in the expected azo coupling of the cyclopropyldiazonium ion, but afforded the corresponding oxaspiropentanes **14**–**17** as products of the addition of diazocyclopropane (**3**) onto one of the carbonyl groups. In addition, the reaction proceeded selectively on the carbonyl groups adjacent to the di- or trifluoromethyl substituents. 1,1-Difluoroacetone reacted analogously with diazocyclopropane (**3**) generated in situ, giving stable 2-(difluoromethyl)-2-methyloxaspiropentane in approximately 50% yield. The resulting oxaspiropentanes **14**–**17**, on heating or in the presence of lithium iodide, rearranged selectively into cyclobutanones **20**–**23**, while in the presence of Al_2O_3 they formed mixtures of approximately equal amounts of the corresponding cyclobutanones and the 1-vinylcyclopropanols **24**–**27**.

Introduction

Fluorinated β-diketones are of interest because of their dual reactivity arising from the presence of two carbonyl groups and their pronounced keto-enol tautomerism, representing great potential for synthesis of new fluorine-containing synthons.[1−3] The interactions of diazo compounds (or diazonium ions) with these compounds are of particular interest because of their ability to react at regions of localized electron density deficiency and/or at the site of maximum nucleophilicity. Azo coupling reactions are known to be the most typical chemical transformations for aromatic diazo compounds and diazonium salts.[4−8] There are examples of azo coupling reactions occurring with the retention of nitrogen atoms in the case of some stable diazocarbonyl compounds.[9,10] The reactions of aliphatic diazo compounds, if generation of diazonium ions is assumed, are generally accompanied by elimination of the nitrogen molecule followed by transformation of the resulting carbocations.[5,11,12] Nevertheless, it appeared that cyclopropyldiazonium ions can undergo transformations highly competitive with deazotation.[11−14] We have recently reported that azo coupling products were obtained by decomposition of *N*-cyclopropyl-*N*-nitrosourea (**1**) with K_2CO_3 in the presence of hydroxynaphthalenes,[15,16] hydroxyquinoline,[15] methyl cyanoacetate,[17] malonodinitrile,[17] pyrazoline derivatives[18] and some β-diketones.[17] It is interesting to note that under the same conditions cyclopropyldiazonium **2** and diazocyclopropane **3** or both can be intermediates in reactions with appropriate substrates, such as **4** and **5**, to afford the products of 1,3-dipolar cycloaddition **6** in the case of unsaturated compounds[19] and the azo coupling products **7** in the case of C−H acids.[17]

It is also known[20−23] that diazocyclopropane generated in situ reacts with some ketones to form oxaspiropentane derivatives or the products of their rearrangement. Treatment of **3** with acetone **8** thus gave dimethyloxaspiropentane **9** (Scheme 1),[20] while reactions between **3** and the carbonyl groups of trispirodecanone[21] and of steroids[22,23] afforded the corresponding oxaspiropentanes, which rearranged to cyclobutanone derivatives under the reaction conditions used. It should be noted that analogous reactions between cyclopropyl-ylides and carbonyl compounds[24−26] and the rearrangements of the resulting oxaspiropentanes have been used in strategies for the synthesis of some antibiotics and of antifungal, tumour-inhibitory and other biologically active substances.[27−31]

It is believed that the initial step of the reaction between a diazo compound and a ketone is an attack on the electron-deficient carbon atom of the C=O group by an aliphatic diazo compound, followed by the elimination of a nitrogen molecule and the cycle closure. In this respect it would be of interest to study the behaviour of some fluorine-containing ketones and β-diketones and their reactivity tendencies in their reactions with diazocyclopropyl intermediates **2** and **3**. For this purpose β-diketones containing a CHF_2 or CF_3 fragment at one of their carbonyl groups and an alkyl, cycloalkyl or heterocycle substituent at the other were used as the substrates.

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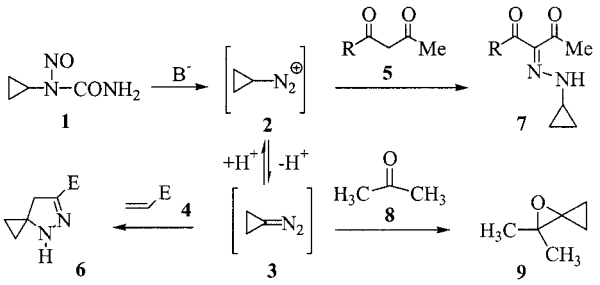
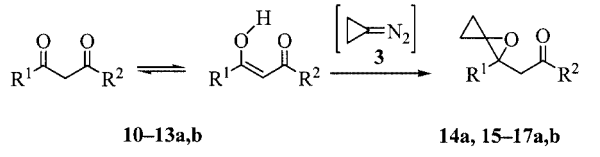


Scheme 1

Results and Discussion

According to their ^{1}H NMR spectra and in agreement with known data[1] all the β-diketones used exist practically completely as keto-enol forms in solution in $CDCl_3$. On account of this, we at first expected that these compounds, as well as the non-fluorinated β-diketones **5**,[17] would show properties of active CH-acids and would undergo azo coupling with the cyclopropyldiazonium ion (**2**). The behaviour of the fluorine-containing diketones **10a**,**b**−**13a**,**b** (Scheme 2), however, proved to differ clearly from that of their non-fluorinated analogues. The decomposition of *N*-cyclopropyl-*N*-nitrosourea (**1**) on treatment with K_2CO_3 containing 20 mol% of H_2O in the presence of difluoro derivatives **10a**−**13a** in a molar ratio of reagents of approximately 1.2:2.4:1 in CH_2Cl_2, for example, resulted in the formation of oxaspiropentanes **14a**−**17a**. In the cases of adamantyl-, cyclopropyl- and pyrazolyl-substituted β-diketones **11a**−**13a** the yields of the oxaspiropentanes **15a**−**17a** were quite high (Table 1).



Scheme 2

Table 1. The formation of oxaspiropentanes **14**−**17** from β-diketones **10**−**13**

Compounds	R^2	Yields (%) R^1 (**a**) CHF_2	R^1 (**b**) CF_3
10a,**b**, **14a**	methyl	38	–
11a,**b**, **15a**,**b**	cyclopropyl	76	17
12a,**b**, **16a**,**b**	1,3-dimethyl-pyrazol-4-yl	84	15
13a,**b**, **17a**,**b**	1-adamantyl	84	16

When the trifluoro-substituted β-diketones **10b**−**13b** were used in these reactions the yields of the corresponding (trifluoromethyl)oxaspiropentanes **15b**−**17b** were significantly decreased (Table 1). Oxaspiropentane **14b** was hardly formed from 1,1,1-trifluoropentane-2,4-dione (**10b**). At the same time, we failed to observe the corresponding azo coupling products in the cases of both di- and trifluoromethyl derivatives **10**−**13**.

It is necessary also to note that the use of 1,1,1,5,5,5-hexafluoropentane-2,4-dione as the substrate under the same conditions resulted neither in products of trapping of diazocyclopropane **3** nor in products of azo coupling with cyclopropyldiazonium (**2**), and that subsequent acidification of the reaction mixture mainly resulted in the separation of the starting keto-enol.

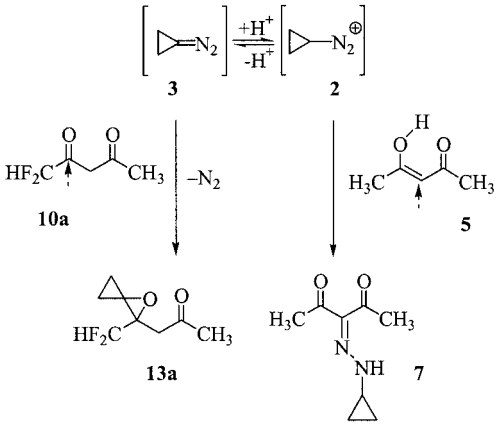
The resulting oxaspiropentanes were isolated as individual compounds and characterized by mass and ^{1}H, ^{13}C and ^{19}F NMR spectroscopy. (Difluoromethyl)oxaspiropentanes **14a**−**17a** were obtained in high purity just by filtration of the reaction mixture through a thin layer of silica gel in CH_2Cl_2. A convenient method of purification of crystalline oxaspiropentanes **16a** and **17a** from insignificant impurities was by recrystallization from hexane. At the same time, attempts to separate oxaspiropentanes **14a**−**17a** by distillation or chromatographic methods were unsuccessful because of partial isomerization (see below). In contrast, (trifluoromethyl)oxaspiropentanes **8b**−**10b** proved to be more stable, and the most convenient method for their purification was preparative TLC on silica gel.

According to the ^{13}C NMR spectra the interaction of intermediate **3** with all studied β-diketones proceeds regioselectively at the carbonyl group adjacent to the di- or trifluoromethyl substituent. Thus, in all cases the C-2 atom of the oxaspiropentane fragment of compounds **14**−**17** exhibited a peak at approximately δ = 60 ppm with a significant spin−spin coupling constant ($^2J_{C,F}$ = 26−30 Hz for compounds **14a**−**17a** and 37 Hz for compounds **15b**−**17b**), whereas the carbonyl carbon atom gave a singlet, indicating remoteness of the fluorine atoms. In the ^{1}H NMR spectra, the methylene protons of all resulting oxaspiropentanes proved to be magnetically non-equivalent, exhibiting two independent doublets with spin−spin coupling constants ($^2J_{H,H}$ = 16.5−17.5 Hz), the difference in chemical shifts being very intense in the case of the adamantyl-containing compounds **17a** and **17b**. The ^{19}F NMR spectra showed fluorine atoms of geminal non-equivalence, with the result that All the (difluoromethyl)oxaspiropentanes **14a**−**17a** exhibited signals appearing as broadened doublets of doublets (spin−spin coupling constant $^2J_{FF}$ = 285−295 and $^2J_{H,F}$ = 55−56 Hz).

The absence of azo coupling products of cyclopropyldiazonium (**2**) with fluorine-containing β-diketones **10a**,**b**−**13a**,**b**, and on the other hand the efficient formation of oxaspiropentanes **14**−**17** are probably due to the electron density distribution in a molecule rather than the rate of enolization of starting diketones, which is high for polyfluorinated β-diketones in comparison with their non-fluorinated counterparts.[1,32,33] The presence of electron-withdrawing fluoromethyl groups is responsible for reduced nucleophilicity of the carbon atom located between two carbonyl groups, so these compounds are inactive in azo coupling with the intermediate **2**. On the other hand, the

significant positive charge on a carbon atom adjacent to a fluoromethyl group facilitates its easy interaction with the nucleophilic carbon atom of diazocyclopropane (**3**), followed by the elimination of a nitrogen molecule and the closure of the oxirane cycle.

Note that diazocyclopropane (**3**) probably attacks the carbon atom of the carbonyl group of the ketone form of the corresponding β-diketones, unlike cyclopropyldiazonium (**2**), which reacts with the enol form (Scheme 3). In the case of non-equivalent carbonyl groups the enolization of β-diketones mainly occurs at the carbon atom bonded to the more electron-deficient substituent,[1] as was demonstrated by ^{13}C NMR.[32] The concentrations of the enol forms of 1,1-difluoropentane-2,4-dione (**10a**) and 1,1,1-trifluoropentane-2,4-dione (**10b**) in $CDCl_3$ are about 95−97% and 99.5%, respectively.[1,33,34] If instability of the diazocyclopropyl intermediates is taken into account, the behaviour of substrates **10b**−**13b** is the limiting factor in the chemical trapping techniques, which causes significant reductions in of yields of oxaspiropentanes **15b**−**17b** in comparison with those of substrates **10a**−**13a**. Probably, hydration of the trifluoromethyl-substituted carbonyl groups of trifluoromethyl derivatives[35] and the easy formation of salts[1] with K_2CO_3 also reduce the possibility of oxaspiropentane formation in this case.

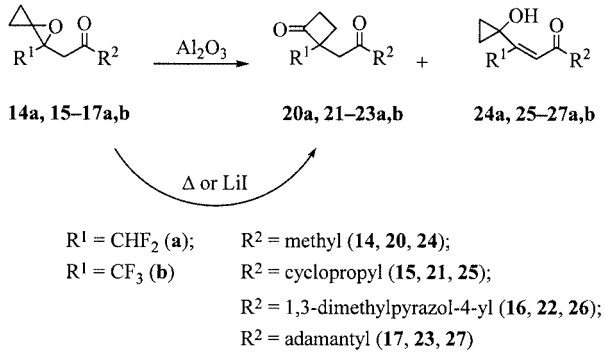


Scheme 3

Oxaspiropentanes are very important intermediates in organic synthesis.[36,37] Their versatility as synthetic blocks is clearly demonstrated by their capability to react with nucleophiles such as PhSeNa[38] and bases[39−41] such as R_2NLi to give cyclopropanols, and to undergo ring-expansion to cyclobutanones on treatment with acidic reagents such as protonic acids, lithium or europium salts[39,42−44] or by thermal treatment.[45,46] It has been found that Grignard reagent-induced ring-expansion of oxaspiropentanes to cyclobutanols occurs through the intermediacy of a cyclobutanone,[47−48] and it has also been noted that the interaction of diazocyclopropane (**3**) generated in situ with the carbonyl groups of trispirodecanone[21] and of some ketosteroids[22,23] affords the corresponding cyclobutanones as a result of the isomerization of unstable oxaspiropentane intermediates.

We thus studied the chemical transformations of the synthesized difluoro- and trifluoro-containing oxaspiropentanes **14**−**17** into the corresponding cyclobutanones and cyclopropanols under different reaction conditions. The di- and (trifluoromethyl)oxaspiropentanes **14**−**17** rearranged into the corresponding cyclobutanones **20**−**23** in high yields on boiling in benzene for 8−10 h or in the presence of LiI (5 mol%) under mild conditions (35°C, CH_2Cl_2, 12 h). Partial isomerization of the difluoro-substituted derivatives **14a**−**17a** took place on silica gel during attempts to separate them by preparative TLC. At the same time, the trifluoromethyl derivatives **15b**−**17b** could be separated by such methods without evident transformation.

Oxaspiropentanes **14**−**17** deposited onto aluminium oxide surfaces behaved in another way. Keeping of difluoro- (**14a**−**17a**) and (trifluoromethyl)oxaspiropentanes **15b**−**17b** in the presence of neutral Al_2O_3 for 20 h and 30 h, respectively, resulted in practically full conversion of the starting compounds **14**−**17**, and in the formation of cyclobutanones **20**−**23** together with vinylcyclopropanols **24**−**27** in approximately equal quantities. The last compounds were isolated in the pure state by preparative TLC and characterized by mass and NMR spectroscopy.



Scheme 4

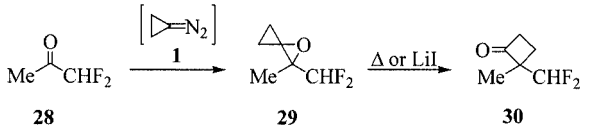
The ^1H NMR spectra of all cyclobutanones obtained showed the signals of exocyclic methylene protons as two doublets with geminal spin−spin coupling constants $^2J_{H,H}$ = 18−19 Hz. In the ^{13}C NMR spectra, each carbonyl group exhibited two downfield signals (δ = 189−212 ppm): a doublet of doublets (spin−spin coupling constant $^3J_{C,F}$ = 3−9 Hz) in the case of compounds **24a**−**27a** and a quadruplet (spin−spin coupling constant $^3J_{C,F}$ = 3−5 Hz) in that of compounds **25b**−**27b**. The ^{19}F NMR spectra of (difluoromethyl)cyclobutanones **20a**−**23a** showed magnetic non-equivalence of the fluorine atoms as a small difference in chemical shifts (Δδ = 1−2 ppm, spin−spin coupling constant $^2J_{FF}$ 284.9−286.6 Hz), in contrast to the trifluoro-substituted cyclobutanones **21b**−**23b**, which gave singlets.

The ^1H NMR spectra of vinylcyclopropanols showed the characteristic set of signals corresponding to the protons of cyclopropane ring in the upfield region, the olefin proton signal at δ = 6.6−7.0 ppm and the broadened signal of the hydroxy group. In the ^{13}C NMR spectra the only signal corresponding to the keto group at δ = 184−208 ppm was

observed in all compounds **24**−**27**. The ^{19}F NMR spectra of the cyclopropanols **24a**−**27a**, in contrast to those of the oxaspiropentanes **14a**−**17a** and the cyclobutanones **20a**−**23a**, revealed only spin-spin interactions of magnetically equivalent fluorine atoms with the CHF_2 group protons (spin−spin coupling constant $^3J_{H,F}$ = 53.3−55.0 Hz). Note that in the IR spectra of compounds **24**−**27** in CCl_4 solution, broad hydroxy group absorption was observed at $\tilde{\nu}$ = 3300−3500 cm^{-1}. In all cases the independence of the signal character of the concentration of the studied solution pointed at the existence of an intramolecular hydrogen bond and, correspondingly, a *cis* orientation of keto group and cyclopropanol fragment. The vinylcyclopropanols **24**−**27** had thus been obtained selectively in their (*E*) forms.

As diazocyclopropane (**3**) had proved to react with acetyl fragments of β-diketones containing fluorine atoms, it was thought it would be interesting to carry out analogous reactions with 1,1-difluoroacetone (**28**). Indeed, employment of ketone **28** as an acceptor of diazo compound **3** resulted in reaction at the carbonyl group and the formation of 1-difluoromethyl-1-methyloxaspiropentane (**29**) in about 50% yield. This reaction proceeds more effectively and selectively than the previously described[20] interaction between acetone itself and diazocyclopropane (**3**) generated in situ from *N*-cyclopropyl-*N*-nitrosourea (**1**) and K_2CO_3 in methanol. The resulting compound **29**, in contrast with other synthesized oxaspiropentanes (among them dimethyloxaspiropentane obtained from acetone), is very stable and can easily be isolated without isomerization by distillation at atmospheric pressure.

The rearrangement of **29** to the corresponding cyclobutanone **30** in 94% yield occurred in the presence of 5 mol% of LiI in CH_2Cl_2 at 40 °C over 12 h. Full consumption of oxaspiropentane **29** was also achieved on heating under less mild conditions (flow reactor, 380−400 °C), but unidentified by-products were observed besides cyclobutanone **30** (yield ≈70%). According to the ^1H NMR spectrum of the reaction mixture the impurities exhibited some signals in aromatic fields.



Scheme 5

At the same time, we failed to obtain the corresponding cyclopropanol from compound **29** in the presence of neutral Al_2O_3. Note that we failed to observe any interaction of cyclobutanones **20**−**23** and cyclopropanols **24**−**27** with diazocyclopropane (**3**) or cyclopropyldiazonium ion (**2**) generated in situ.

Conclusion

Treatment of di- and trifluoro-containing β-diketones **10**−**13** with diazocyclopropane (**3**) generated in situ by the decomposition of *N*-cyclopropyl-*N*-nitrosourea (**1**) in the presence of moist K_2CO_3 proceed at the carbonyl group bonded to the di- or trifluoromethyl substituent and result in the formation of the corresponding oxaspiropentanes **14**−**17**. The yields of oxaspiropentanes obtained from 1,1-difluoroalkane-2,4-diones are significantly higher than those obtained in the case of the corresponding 1,1,1-trifluoroalkanediones and achieve values of 80−84%. The observed transformations differ from the reactions of non-fluorinated β-dicarbonyl compounds, when azo coupling at the active methylene group is the most typical process. This difference is probably related to the electron density distributions in the molecules of β-dicarbonyl compounds and determines which intermediate, diazocyclopropane (**3**) or cyclopropyldiazonium ion (**2**), will react with carbonyl (electrophilic) or methylene (nucleophilic) centres of the molecule.

Experimental Section

General Remarks: The ^1H, ^{13}C and ^{19}F NMR spectra were recorded with Bruker AC 200 (^1H, 200 MHz, ^{19}F, 188.3 MHz and ^{13}C, 50.3 MHz) and Bruker AM 300 (^1H, 300 MHz and ^{13}C, 75.5 MHz) instruments on $CDCl_3$ solutions. The ^{13}C NMR spectra were recorded with broadband decoupling of ^1H nuclei. Chemical shifts in the ^1H and ^{13}C spectra are given from TMS as internal standard, and δ_F values in the ^{19}F NMR spectra are quoted relative to CCl_3F. Mass spectra were obtained with a Finnigan MAT INCOS-50 instrument (EI, 70 eV, direct injection). IR spectra were recorded with a Bruker IFS-113v instrument on CCl_4 solutions or KBr tablets. Elemental analyses were performed with a Perkin−Elmer (Series II) C,H,N-analyzer 2400. Melting points (uncorrected) were determined in capillary tubes. The preparative TLC was carried out on silica gel 60 (0.040−0.063 mm) or neutral Al_2O_3 (Merck). Chemically pure potassium carbonate, containing approx. 20% H_2O as a result of drying, acetyladamantane, ethyl trifluoroacetate, ethyl difluoroacetate (Aldrich), and all solvents used were of commercial quality. *N*-Cyclopropyl-*N*-nitrosourea,[49] 1,1-difluoroacetone,[50] β-diketones[51] and 1-(1,3-dimethyl-1*H*-pyrazol-4-yl)-1-ethanone,[52] the starting material for the synthesis of diketones **12**, were obtained by known procedures. The characteristics of 1,1-difluoro-2,4-pentanedione[51] and 1-cyclopropyl-4,4,4-trifluoro-1,3-butanedione[53] corresponded to the literature data.

1-Cyclopropyl-4,4-difluoro-1,3-butanedione (11a) (enol form): Yield 70% (15.2 g), colorless liquid, b.p. 91−94°C/7 Torr. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.15 (m, 4 H, CH_2CH_2), 1.80 (m, 1 H, CH), 5.98 (t, *J* = 54.2 Hz, 1 H, CHF_2), 6.03 (s, 1 H, 3-H), 14.08 (s, 1 H, OH) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −130.9 (br. d, $J_{H,F}$ = 54.8, CHF_2) ppm. EIMS (70 eV): *m/z* (%) = 163(9) $[M + H]^+$, 147 (1) $[M - CH_3]^+$, 111 (20), 69 (100), 51 (20), 41 (56). $C_7H_8F_2O_2$ (162.1): calcd. C 51.86, H 4.97; found C 51.85, H 4.96.

4,4-Difluoro-1-(1,3-dimethyl-1*H*-pyrazol-4-yl)-1,3-butanedione (12a): Yield 53% (9.5 g) colourless solid, b.p. 170−175 °C/7 Torr, m.p. 48−50 °C. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.50 (s, 3 H, Me), 3.89 (s, 3 H, Me), 6.00 (t, *J* = 54.4 Hz, 1 H, CHF_2), 6.14 (s, 1 H, 3-H), 7.87 (s, 1 H, 5′-H) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −130.4 (br. d, $J_{H,F}$ = 55.0, CHF_2) ppm. EIMS (70 eV): *m/z* (%) = 216 (65) $[M]^+$, 165 (100), 123 (50), 97 (23), 69

(16), 51 (15), 42 (15). $C_9H_{10}F_2N_2O_2$ (216.2): calcd. C 50.00, H 4.66, N 12.96; found C 50.13, H 4.65, N 12.93.

1-(1,3-Dimethyl-1*H*-pyrazol-4-yl)-4,4,4-trifluoro-1,3-butanedione (12b): Yield 49% (9.3 g), pink solid, b.p. 160−162 °C, m.p. 49−53 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.25 (s, 1 H, OH), 2.49 (s, 3 H, Me), 3.89 (s, 3 H, NMe), 6.16 (s, 1 H, 3-H), 7.88 (s, 1 H, 5-H) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −75.8 (br. s, CF_3) ppm. EIMS (70 eV): *m*/*z* (%) = 234 (61) $[M]^+$, 214 (1) $[M - HF]^+$, 165 (61), 123 (100), 97 (21), 69 (25), 42 (15). $C_9H_9F_3N_2O_2$ (234.2): calcd. C 46.16, H 3.87, N 11.96; found C 46.01, H 3.86, N 11.94.

1-(1-Adamantyl)-4,4-difluoro-1,3-butanedione (13a): Yield 70% (19.2 g), colourless, oily liquid, b.p. 182−184C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.75 (m, 12 H, Ad), 2.08 (m, 3 H, Ad), 5.90 (t, *J* = 54.5 Hz, 1 H, CHF_2), 5.95 (s, 1 H, 3-H), 13.8 (br. s, OH) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −130.4 (br. d, $J_{H,F}$ = 54.5, CHF_2) ppm. EIMS (70 eV): *m*/*z* (%) = 255 (22) $[M - H]^+$, 213 (7) $[M - C_3H_7]^+$, 196 (10), 151 (62), 135 (100), 121 (51), 107 (22), 93 (40), 73 (60), 69 (38), 55 (20), 51 (32), 41 (39). $C_{14}H_{18}F_2O_2$ (256.3): calcd. C 65.61, H 7.08; found C 65.75, H 7.07.

1-(1-Adamantyl)-4,4,4-trifluoro-1,3-butanedione (13b): Yield 68% (17.8 g), colourless solid, b.p. 164−165 °C/7 Torr, m.p. 30−32 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.75 (m, 12 H, Ad), 2.08 (m, 3 H, Ad), 5.95 (s, 1 H, 3-H), 13.8 (br. s, OH) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F, 25 °C): δ = −76.2 (br. s, CF_3) ppm. EIMS (70 eV): *m*/*z* (%) = 274 (17) $[M]^+$, 246 (8) $[M - CO]^+$, 205 (5) $[M - CF_3]^+$, 135 (100), 93 (14), 69 (14). $C_{14}H_{17}F_3O_2$ (274.3): calcd. C 61.31, H 6.25; found C 61.43, H 6.24.

Preparation of Oxaspiropentanes 7−10. General Procedure: K_2CO_3 (2.4 mmol) was added at 0 °C in three portions over 45 min to a stirring solution of fluorine-containing β-diketone (**10**−**13**, 1 mmol) and *N*-cyclopropyl-*N*-nitrosourea (**2**, 1.2 mmol) in CH_2Cl_2 (5 mL) and the reaction mixture was additionally stirred for 1.5 h. It was then rapidly passed through a thin layer of silica gel (1.0 cm) and washed with CH_2Cl_2 (all reagent amounts can be adjusted in proportion to weight of diketone used). The solvent was evaporated in vacuo to provide the oxaspiropentanes **14**−**17**. The resulting compounds **16a** and **17a** were obtained as needles by recrystallization from hexane, and compounds **16b**−**17b** were isolated by preparative TLC on silica gel.

2-(Difluoromethyl)-2-(2-oxopropyl)-1-oxaspiro[2.2]pentane (14a): Yield 38% (307.0 mg), yellowish oil. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.11 (m, 4 H, 4-H and 5-H), 2.20 (s, 3 H, Me), 2.84 and 3.23 (both br.d, ^2J = 16.8 Hz, 1 H, CH_2), 5.76 (t, $J_{H,F}$ = 55.2 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 1.5 and 2.3 (both s, C-4 and C-5), 30.5 (s, Me), 42.4 (s, CH_2), 59.7 (dd, $^2J_{CF}$ = 30.0, 26.4 Hz, C-2), 61.2 (dd, $^3J_{CF}$ = 2.0, 5.8 Hz, C-3), 115.2 (t, $^1J_{CF}$ = 242 Hz, CHF_2), 203.5 (C, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F, 25 °C): δ = −125.4 and −123.3 (both dd, J_{FF} = 290.0, $J_{H,F}$ = 55.2 Hz, CHF_2) ppm. EIMS (70 eV): *m*/*z* (%) = 177 (1) $[M + H]^+$, 159 (2) $[M - H_2O]^+$, 105 (10), 97 (10), 85 (20), 84 (27), 70 (20), 57 (56), 56 (60), 43 (100). $C_8H_{10}F_2O_2$ (176.2): calcd. C 54.55, H 5.72; found C 54.75, H 5.79.

2-(2-Cyclopropyl-2-oxoethyl)-2-(difluoromethyl)-1-oxaspiro[2.2]-pentane (15a): Yield 76% (320 mg), yellowish oil. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.08 (m, 8 H, all CH_2 in cyclopropane fragments), 2.30 (m, 1 H, CH), 2.95 (d.t, ^2J = 17.2 and 1.2 Hz, 1 H) and 3.40 (d, ^2J = 17.2 Hz, 1 H, CH_2), 5.81 (td, $J_{H,F}$ = 55.0 and 1.3 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 1.6 and 2.4 (both s, C-4 and C-5), 11.3 and 11.6 (both s, C-2′ and C-3′), 21.0 (s, CH), 42.4 (s, CH_2), 59.7 (dd, $^2J_{CF}$ = 26.4 and 29.8 Hz, C-2), 61.2 (dd, $^3J_{CF}$ = 3.0 and 6.0 Hz, C-3), 115.1 (dd, $^1J_{CF}$ = 242.0 and 243.0 Hz, CHF_2), 205.7 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −126.3 and −123.8 (both dd, J_{FF} = 295.0, $J_{H,F}$ = 55.0 Hz, CHF_2) ppm. EIMS (70 eV): *m*/*z* (%) = 203 (10) $[M + H]^+$, 181 (3) $[M - HF - H]^+$, 162 (2), 111 (91), 69 (100), 51 (15), 41 (80). $C_{10}H_{12}F_2O_2$ (202.2): calcd. C 59.40, H 5.98; found C 59.28, H 5.83.

2-(2-Cyclopropyl-2-oxoethyl)-2-(trifluoromethyl)-1-oxaspiro[2.2]-pentane (15b): The compound was isolated by preparative TLC (silica gel, eluent: benzene/chloroform, 2:1, R_f = 0.63), yield 17% (188 mg), yellowish oil. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.90−1.40 (m, 8 H, all CH_2 of cyclopropyl fragments), 2.02 (tt, *J* = 7.7, *J* = 4.4 Hz, 1 H, CH), 2.99 (dq, *J* = 16.5, *J* = 0.6 Hz, 1 H), 3.48 (d, *J* = 16.5 Hz, 1 H, CH_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 2.5 and 3.1 (both s, C-4 and C-5), 11.4 and 11.8 (both s, C-2′ and C-3′), 21.1 (s, C-1′), 43.1 (s, CH_2), 59.2 (q, $^2J_{CF}$ = 37.0 Hz, C-2), 61.0 (q, $^3J_{CF}$ = 2.5 Hz, C-3), 123.5 (q, $^1J_{CF}$ = 279.0 Hz, CF_3), 204.2 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −74.3 (br. s, CF_3) ppm. EIMS (70 eV): *m*/*z* (%) = 221 (1) $[M + H]^+$, 203(1) $[M - OH]^+$, 189 (1) $[M - OMe]^+$, 83 (9), 69 (100), 41 (66). $C_{10}H_{11}F_3O_2$ (220.2): calcd. C 54.55, H 5.04; found C 54.69, H 4.97.

2-(Difluoromethyl)-2-[2-(1,3-dimethyl-1*H*-pyrazol-4-yl)-2-oxoethyl]-1-oxaspiro[2.2]pentane (16a): Yield 84% (290 mg), orange needles, m.p. 55−57 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.15 (m, 4 H, 4-H and 5-H), 2.44 (s, 3 H, Me), 3.07 (dd, ^2J = 16.1, *J* = 1.5 Hz, 1 H, CH_2) and 3.58 (d, ^2J = 16.1 Hz, 1 H, CH_2), 3.87 (s, 3 H, NMe), 5.88 (dd, $J_{H,F}$ = 54.8 and 55.8 Hz, 1 H, CHF_2), 7.81 (s, 1 H, =CH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 2.0 and 2.5 (both s, C-4 and C-5), 14.1 (s, Me), 39.1 (s, CH_2), 40.2 (s, NMe), 60.0 (dd, $^2J_{CF}$ = 26.0, 29.5 Hz, C-2), 61.6 (dd, $^3J_{CF}$ = 3.0 and 6.0, C-3), 115.3 (dd, $^1J_{CF}$ = 243.0 and 244.0 Hz, CHF_2), 120.4 (s, C-4′), 134.8 (s, C-5′), 151.3 (s, C-3′), 188.3 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$): δ = −126.2 and −125.0 (both dd, $^2J_{FF}$ = 286.0, $^2J_{H,F} \approx$ 55.2 Hz, CHF_2) ppm. EIMS (70 eV): *m*/*z* (%) = 221 (1) $[M - HF - Me]^+$, 123 (100), 51 (8), 42 (11). $C_{12}H_{14}F_2N_2O_2$ (256.2): calcd. C 56.25, H 5.51, N 10.93; found C 56.16, H 5.44, N 10.85.

2-[2-(1,3-Dimethyl-1*H*-pyrazol-4-yl)-2-oxoethyl]-2-(trifluoromethyl)-1-oxaspiro[2.2]pentane (16b): The compound was isolated by preparative TLC (silica gel, eluent: ether, R_f = 0.47), yield 15% (170 mg), pink needles, m.p. 57−58 °C. −^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.12 and 1.30 ppm(both m, 2 H, CH_2CH_2), 2.44 (s, 3 H, Me), 3.12 (dq, *J* = 16.0, *J* = 1.0 Hz, 1 H) and 3.64 (d, *J* = 16.0 Hz, 1 H, CH_2), 3.86 (s, 3 H, Me), 7.81 (s, 1 H, 5′-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 2.6 and 3.0 (both s, CH_2CH_2), 14.1 (s, Me), 40.2 (s, Me), 40.6 (s, CH_2), 59.4 (q, $^2J_{CF}$ = 37.0 Hz, C-2), 62.1 (q, $^3J_{CF}$ = 2.5 Hz, C-3), 120.4 (s, C-4′), 123.6 (q, $^1J_{CF}$ = 276.0 Hz, CF_3), 134.7 (s, C-5′), 151.3 (s, C-3′), 187.3 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −74.2 (br. s, CF_3) ppm. EIMS (70 eV): *m*/*z* (%) = 274 (51) $[M]^+$, 245 (1) $[M - CHO]^+$, 123 (100), 97 (19), 85 (29), 71 (47), 57 (83), 43 (91). $C_{12}H_{13}F_3N_2O_2$ (274.2): calcd. C 52.56, H 4.78, N 10.22; found C 52.38, H 4.70, N 10.11.

2-[2-(1-Adamantyl)-2-oxoethyl]-2-(difluoromethyl)-1-oxaspiro[2.2]-pentane (17a): Yield 84% (350 mg), colourless needles, m.p. 68−70 °C. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.12 (m, 4 C, 4-H and 5-H), 1.77 (m, 12 H, Ad), 2.08 (m, 3 H, Ad), 2.69 (dd, ^2J = 17.5, *J* = 1.8 Hz, 1 H) and 3.53 (d, ^2J = 17.5 Hz, 1 H, CH_2), 5.85 (t, $J_{H,F}$ = 55.5 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz,

$CDCl_3$): δ = 1.9 and 2.7 (both s, C-4 and C-5), 27.8, 36.4, 37.9 and 46.7 (all s, Ad), 36.6 (s, CH_2), 60.8 (dd, $^2J_{CF}$ = 26.5, 29.0 Hz, C-2), 61.5 (dd, $^3J_{CF}$ = 3.0 and 6.0, C-3), 114.9 (dd, $J_{C,F}$ = 242 and 244 Hz, CHF_2), 206.1 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −124.7 and −127.3 (dd, J_{FF} = 294, $J_{H,F}$ = 55.5 Hz, CHF_2) ppm. EIMS (70 eV): *m/z* (%) = 296 (10) $[M]^+$, 277 (1) $[M - F]^+$, 256 (8), 245 (83), 135 (100), 93 (19), 79 (21). $C_{17}H_{22}F_2O_2$ (296.4): calcd. C 68.90, H 7.48; found C 68.81, H 7.50.

2-[2-(1-Adamantyl)-2-oxoethyl]-2-(trifluoromethyl)-1-oxaspiro[2.2]-pentane (17b): Separated by preparative TLC (silica gel, eluent: ethyl acetate/heptane, 1:4.5, R_f = 0.59), yield 16% (160 mg) colourless needles, m.p. 73−75 °C. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.10 and 1.30 ppm(both m, 2 + 2 H, H-4 and H-5), 1.70 (m, 12 H, Ad), 2.00 (m, 3 H, Ad), 2.62 (br. d, *J* = 17.5 Hz, 1 H) and 3.68 (d, *J* = 17.5 Hz, 1 H, CH_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 2.6 and 3.2 (both s, C-4 and C-5), 27.8, 36.5, 38.2 and 46.7 (all s, Ad), 37.9 (s, CH_2), 60.0 (q, $^2J_{C,F}$ = 36.9 Hz, C-2), 62.3 (q, $^3J_{C,F}$ = 2.6, C-3), 123.5 (q, $^1J_{C,F}$ = 278.0 Hz, CHF_2), 208.4 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −73.9 (br. s, CF_3) ppm. EIMS (70 eV): *m/z* (%) = 314 (1) $[M]^+$, 297 (1) $[M - OH]^+$, 269 (1) $[M - OH - CO]^+$, 135 (100), 107 (09), 93 (18), 79 (23), 67 (11), 55 (12), 41 (20). $C_{17}H_{21}F_3O_2$ (314.3): calcd. C 64.96, H 6.73; found C 64.83, H 6.61.

2-(Difluoromethyl)-2-methyl-1-oxaspiro[2.2]pentane (29): *N*-Cyclopropyl-*N*-nitrosourea (**2**, 3.43 g, 0.027 mol) and K_2CO_3 (9.99 g, 0.057 mol) were added alternately in five−six portions at 4 °C over 1 h to a stirring solution of the difluoroacetone **28** (1.90 g, 0.02 mol) in CH_2Cl_2 (15 mL). The mixture was then stirred for an additional 1 h. After warming to room temperature the reaction mixture was passed through a thin layer of Al_2O_3 (1.0 cm), washed with CH_2Cl_2, dried with anhydrous $MgSO_4$ and distilled in vacuo. The oxaspiropentane **29** (1.34 g, 50%) was obtained as colourless liquid, b.p. 115−118°C. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.10 (m, 4 H, H-4 and H-5), 1.52 (s, 3 H, Me), 5.39 (dd, *J* = 59.0, *J* = 55.6 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 1.0 and 2.6 (both s, C-4 and C-5), 12.3 (d, $^3J_{C,F}$ = 1.4 Hz, Me), 20.1 (s, C-3), 61.6 (d, $^2J_{C,F}$ = 62.0 Hz, C-2), 116.8 (dd, $^1J_{CF}$ = 245 and 242 Hz, CHF_2) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −125.3 (br. dd, J_{FF} = 299.0, $J_{H,F}$ = 59.0 Hz, CHF_2), −121.3 (br. dd, 1F, J_{FF} = 299.0, $J_{H,F}$ = 55.6 Hz, CHF_2) ppm. EIMS (70 eV): *m/z* (%) = 134 (2) $[M]^+$, 114 (3) $[M - HF]^+$, 106 (33) $[M - CO]^+$, 83 (37), 77 (64), 55 (77), 51 (59), 43 (100), 39 (95), 33 (11). $C_6H_8F_2O$ (134.1): calcd. C 53.73, H 6.01; found C 53.56, H 5.89.

2-(Difluoromethyl)-2-methylcyclobutanone (30): LiI (0.024 g, 0.18 mmol) was added to a solution of 1-difluoromethyl-1-methoxyoxaspiropentane **29** (0.54 g, 3.6 mmol) in CH_2Cl_2 (5 mL) and the mixture was kept at 40°C for 12 h. The liquid was then distilled at atmospheric pressure, and 2-difluoromethyl-2-methylcyclobutanone (**30**, 530 mg, 95%) was obtained as a colourless liquid, b.p. 138−140°C. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.32 (t, *J* = 0.6 Hz, 3 H, Me), 1.82 (m, 1 H, 3-H[a]), 2.47 (ddd, *J* = 11.9, *J* = 10.0, *J* = 7.5 Hz, 1 H, 3-H[b]), 3.12 (m, 2 H, 4-H), 5.75 (t, *J* = 55.7 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.9 (dd, $^3J_{C,F}$ = 6.0, 3.5 Hz, Me). 19.0 (t, $^3J_{C,F}$ = 3.7 Hz, C-3), 44.6 (s, C-4), 67.0 (t, $^2J_{C,F}$ = 21.0, C-2), 115.5 (dd, $^1J_{C,F}$ = 246 and 242 Hz, CHF_2), 207.0 (dd, $^3J_{C,F}$ = 7.1, 9.2 Hz, C-1) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −127.8 and −123.3 (br. dd, J_{FF} = 285.0, $J_{H,F}$ = 55.7 Hz, CHF_2) ppm. IR (CCl_4): $\tilde{\nu}$ = 1788 (C=O) cm^{-1}. EIMS (70 eV): *m/z* (%) = 134 (12) $[M]^+$, 114 (11) $[M - HF]^+$, 106 (16) $[M - CO]^+$, 97 (09), 84 (41), 77 (30), 70 (22), 55 (50), 42 (100) $[C_3H_6]^+$. $C_6H_8F_2O$ (134.1): calcd. C 53.73, H 6.01; found C 53.52, H 5.87.

Preparation of Fluorinated Cyclobutanones 20−23

General Procedure A: Lithium iodide (0.18 mmol) was added to a solution of oxaspiropentane (**14**−**17**, 3.6 mmol) in CH_2Cl_2 (5 mL), and the mixture was kept at 40 °C for 10 h. It was then passed through a thin layer of silica gel (1 cm), and the solvent was evaporated in vacuo. Cyclobutanones **20**−**23** were obtained in 95−97% yields.

General Procedure B: A solution of oxaspiropentane (**14**−**17**, 3.6 mmol) in benzene (5 mL) was boiled for 8−10 h. The solvent was then evaporated in vacuo, and the reaction mixture was purified by preparative TLC on a neutral Al_2O_3. Cyclobutanones **20**−**23** were obtained in 90−95% yields.

2-Difluoromethyl-2-(2-oxopropyl)cyclobutanone (20a): Method A, yield 95% (81 mg); method B, yield 90% (75 mg). Yellowish oil, eluent: hexane/ether (1:1), R_f = 0.53. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.08 and 2.30 (both m, 1 + 1 H, 3-H), 2.18 (s, 3 H, Me), 2.98 and 3.06 (both d, *J* = 19.0 Hz, 1 + 1 H, CH_2), 3.12 (m, 1 H) and 3.29 (ddd, *J* = 18.3, 10.1, 5.8 Hz, 1 H, 4-H), 5.85 (t, *J* = 55.9 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 17.2 (t, $^3J_{CF}$ = 3.8, C-3), 29.6 (s, Me), 43.9 (t, $^3J_{CF}$ = 4.0 Hz, CH_2), 45.6 (s, C-4), 67.1 (t, $^2J_{CF}$ = 19.5 Hz, C-2), 115.1 (t, $^1J_{CF}$ = 245 Hz, CHF_2), 204.6 (s, CO), 205.7 (dd, $^3J_{CF}$ = 4.0, 5.0 Hz, C-1) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −126.4 and −125.1 (both br. dd, J_{FF} = 285, $J_{H,F}$ = 55.9 Hz, CHF_2) ppm. EIMS (70 eV): *m/z* (%) = 161 (1) $[M - Me]^+$, 113 (12), 85 (10), 55 (21), 51 (10), 43 (100), 31 (17), 31 (18), 30 (42). $C_8H_{10}F_2O_2$ (176.2): calcd. C 54.55, H 5.72; found C 54.73, H 5.81.

2-(2-Cyclopropyl-2-oxoethyl)-2-(difluoromethyl)cyclobutanone (21a): Method A, yield 96% (96 mg); method B, yield 91% (91 mg). Yellowish oil, eluent: hexane/ether (1:1), R_f = 0.46. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.04 (m, 4 H, CH_2CH_2 of cyclopropyl), 1.92 (m, 1 H, CH), 2.05 (m, 1 H) and 2.29 (ddd, *J* = 12.0, 10.5, 6.1 Hz, 1 H, 3-H), 3.07 (m, 1 H) and 3.29 (ddd, *J* = 18.3, 10.0, 5.8 Hz, 1 H, 4-H), 3.11 and 3.18 (both d, *J* = 19.0 Hz, 1 + 1 H, CH_2), 5.85 (t, *J* = 56.2 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 11.2 and 11.3 (both s, CH_2CH_2 of cyclopropyl), 17.1 (t, $^4J_{CF}$ = 3.8 Hz, C-3), 20.3 (s, CH), 43.8 (t, $^3J_{CF}$ = 4.5 Hz, CH_2), 45.6 (s, C-4), 67.2 (t, $^2J_{CF}$ = 19.3 Hz, C-2), 115.1 (t, $^1J_{CF}$ = 245 Hz, CHF_2), 205.7 (dd, $^3J_{CF}$ = 4.0, 6.0 Hz, C-1), 206.4 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −126.3 and −125.0 (both dd, J_{FF} = 285, $J_{H,F}$ = 56.2 Hz, CHF_2) ppm. EIMS (70 eV): *m/z* (%) = 202 (1) $[M]^+$, 181 (4) $[M - HF - H]^+$, 151 (10), 135 (18), 84 (20), 69 (100), 51 (13), 41 (69). $C_{10}H_{12}F_2O_2$ (202.2): calcd. C 59.40, H 5.98; found C 59.31, H 6.08.

2-(2-Cyclopropyl-2-oxoethyl)-2-(trifluoromethyl)cyclobutanone (21b): Method A, yield 95% (27 mg); method B, yield 90% (38 mg). Yellowish oil, eluent: heptane/ether (1:1), R_f = 0.64. ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.03 (m, 4 H, CH_2CH_2 of cyclopropyl), 1.95 (m, 1 H, CH), 2.00 and 2.30 (both m, 1 + 1 H, 3-H), 3.19 (m, 2 H, 4-H), 3.23 and 3.40 (both d, *J* = 18.5 Hz, 1 + 1 H, CH_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 11.7 and 11.8 ppm(both s, CH_2CH_2 of cyclopropyl), 18.3 (q, $^3J_{CF}$ = 2.1 Hz, C-3), 20.3 (s, CH), 44.2 (q, $^3J_{CF}$ = 2.1, CH_2), 46.4 (s, C-4), 67.0 (q, $^2J_{CF}$ = 25.2 Hz, C-2), 125.3 (q, $^1J_{CF}$ = 281 Hz, CF_3), 201.7 (q, $^3J_{CF}$ = 2.5, C-1), 206.2 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −73.5 (br. s, CF_3) ppm. EIMS (70 eV): *m/z* (%) = 221 (39) $[M + H]^+$, 203 (5) $[M - OH]^+$, 103 (10), 69 (100),

41 (45). $C_{10}H_{11}F_3O_2$ (220.2): calcd. C 54.55, H 5.04; found C 54.36, H 4.90.

2-(Difluoromethyl)-2-[2-(1,3-dimethyl-1*H*-pyrazol-4-yl)-2-oxoethyl]-cyclobutanone (22a): Method A, yield 97% (78 mg); method B, yield 95% (65 mg). Pink needles, m.p. 58−60°C, eluent: ether, R_f = 0.3. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.18 (m, 1 H, 3-H^a), 2.35 (ddd, J = 12.0, 10.5, 5.8 Hz, 1 H, 3-H^b), 2.42 (s, 1 H, Me), 3.15 (m, 1 H, 4-H^a), 3.25 and 3.31 (d, J = 18.0 Hz, 1 + 1 H, CH_2), 3.38 (ddd, J = 18.5, 10.3, 5.8 Hz, 1 H, 4-H^b), 3.89 (s, 3 H, NMe), 5.93 (t, J = 55.7 Hz, 1 H, CHF_2), 7.83 (s, 1 H, =CH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.0 (s, Me), 17.6 (t, $^3J_{C,F}$ = 3.7 Hz, C-3), 39.1 (s, C-4), 41.2 (t, $^3J_{C,F}$ = 4.1 Hz, CH_2), 45.8 (s, NMe), 67.4 (t, $^2J_{CF}$ = 19.4 Hz, C-2), 115.5 (t, $^1J_{CF}$ = 245.0 Hz, CHF_2), 119.6 (s, C-4′), 134.3 (s, C-5′), 151.2 (s, C-3′), 189.9 (s, CO), 206.0 (dd, $^3J_{C,F}$ = 5.5, $^3J_{C,F}$ = 4.5, C-1) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −126.2 and −125.0 (both br. dd, J_{FF} = 286.0, $J_{F,H}$ = 55.7 Hz, CHF_2) ppm. EIMS (70 eV): *m/z* (%) = 256 (4) $[M]^+$, 228 (5) $[M - N_2]^+$, 205 (24) $[M - HF - CO]^+$, 123 (100). $C_{12}H_{14}F_2N_2O_2$ (256.2): calcd. C 56.25, H 5.51, N 10.93; found C 56.12, H 5.60, N 10.80.

2-[2-(1,3-Dimethyl-1*H*-pyrazol-4-yl)-2-oxoethyl]-2-(trifluoromethyl)-cyclobutanone (22b): Method A, yield 96% (23 mg); method B, yield 90% (37 mg). Pink needles, m.p. 59−62°C, eluent: ether, R_f = 0.33. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.31 (m, 2 H, 3-H), 2.44 (s, 3 H, Me), 3.15 and 3.55 (both m, 1 + 1 H, 4-H), 3.20 and 3.50 (both d, J = 18.0 Hz, 1 + 1 H, CH_2), 3.89 (s, 3 H, NMe), 7.80 (s, 1 H, =CH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.0 (s, Me), 18.4 (q, $^3J_{C,F}$ = 2.1 Hz, C-3), 39.1 (s, C-4), 41.5 (q, $^3J_{C,F}$ = 2.1 Hz, CH_2), 46.4 (s, NMe), 66.9 (q, $^2J_{C,F}$ = 24.9 Hz, C-2), 119.2 (s, C-4′), 125.4 (q, $^1J_{C,F}$ = 280.0 Hz, CF_3), 134.3 (s, C-5′), 151.3 (s, C-3′), 189.2 (s, CO), 201.8 (q, $^3J_{C,F}$ = 2.5, C-1) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −73.2 (br. s, CF_3) ppm. EIMS (70 eV): *m/z* (%) = 274 (1) $[M]^+$, 245 (1) $[M - CHO]^+$, 123 (100), 49 (10), 42 (20). $C_{12}H_{13}N_2F_3O_2$ (274.2): calcd. C 52.56, H 4.78, N 10.22; found C 52.41, H 4.67, N 10.28.

2-[2-(1-Adamantyl)-2-oxoethyl]-2-(difluoromethyl)cyclobutanone (23a): Method A, yield 97% (98 mg); method B, yield 95% (95 mg). Colourless needles, m.p. 72−74 °C, eluent: heptane/ether (1:1), R_f = 0.67. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.75 m, 12 H, Ad), 1.95 (m, 1 H, 3-H^a), 2.09 (m, 3 H, Ad), 2.30 (ddd, J = 18.4, 10.2, 5.8 Hz, 1 H, 3-H^b), 2.99 and 3.07 (both d, J = 18.8 Hz, 1 + 1 H, CH_2), 3.12 (m, 1 H, 4-H^a), 3.13 (ddd, J = 18.4, 10.2, 5.8 Hz, 1 H, 4-H^b), 5.85 (t, J = 55.8 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 17.4 (t, $^3J_{C,F}$ = 3.9 Hz, C-3), 27.7, 36.3, 38.0 and 45.6 (all s, Ad), 38.0 (dd, $^3J_{C,F}$ = 3.3, 4.7 Hz, CH_2), 46.0 (s, C-4), 67.1 (t, $^2J_{C,F}$ = 19.3 Hz, C-2), 115.3 (t, $^1J_{C,F}$ = 245.0 Hz, CHF_2), 206.0 (dd, $^3J_{C,F}$ = 4.0, 6.0 Hz, C-1), 211.8 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −126.2 and −124.8 (both br. dd, J_{FF} = 286.0, $J_{H,F}$ = 55.8 Hz, CHF_2) ppm. IR (KBr): $\tilde{\nu}$ = 1672, 1625 cm^{-1} (C=O). EIMS (70 eV): *m/z* (%) = 296 (1) $[M]^+$, 279 (1) $[M - OH]^+$, 267 (1) $[M - CHO]^+$, 245 (10), 149 (11), 135 (100), 107 (11), 93 (22), 83 (15), 79 (32). $C_{17}H_{22}F_2O_2$ (296.4): calcd. C 68.90, H 7.48; found C 68.82, H 7.45.

2-[2-(1-Adamantyl)-2-oxoethyl]-2-(trifluoromethyl)cyclobutanone (23b): Method A, yield 96% (28 mg); method B, yield 93% (35 mg). Colourless needles, m.p. 75−77 °C, eluent: heptane/ether (1:1), R_f = 0.70. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.65 (m, 12 H, Ad), 2.06 (m, 4 H, Ad and 3-H^a), 2.16 (m, 1 H, 3-H^b), 3.16 and 3.21 (both d, J = 19.0 Hz, 1 + 1 H, CH_2) 3.17 (m, 1 H, 4-H^a), 3.48 (ddd, J = 18.5, 11.0, 5.7 Hz, 1 H, 4-H^b) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 18.2 (q, $^3J_{C,F}$ = 2.1 Hz, C-3), 27.7, 36.1, 38.0 and 46.2 (all s, Ad), 38.4 (q, $^3J_{C,F}$ = 1.8 Hz, CH_2), 46.0 (s, C-4), 66.7 (q, $^2J_{C,F}$ = 24.5 Hz, C-2), 125.3 (q, $^1J_{C,F}$ = 280.0 Hz, CF_3), 201.6 (q, $^3J_{C,F}$ = 3.9 Hz, C-1), 211.4 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −73.2 (br. s, CF_3) ppm. EIMS (70 eV): *m/z* (%) = 314 (1) $[M]^+$, 245 (1) $[M - CF_3]^+$, 135 (100), 123 (13), 93 (12), 84 (56), 47 (18). $C_{17}H_{21}F_3O_2$ (314.3): calcd. C 64.96, H 6.73; found C 64.82, H 6.62.

Procedure for the Preparation of Cyclopropanols 24−27: Oxaspiropentanes **14−17** in ether solution were deposited on the surface of neutral Al_2O_3 (7−10 fold excess by weight), and the obtained suspension was kept at room temperature for approximately 20 h in the case of (difluoromethyl)oxaspiropentanes **14a−17a** and 30 h in the case of trifluoromethyl derivatives **15b−17b**. The organic compounds were then washed out with CH_2Cl_2 and products of isomerization were separated by preparative TLC on Al_2O_3. Cyclobutanones **20−23** and vinylcyclopropanols **24−27** were obtained in 93−97% overall yields (approx. 1:1, except for cyclobutanone **21b** and cyclopropanol **25b**, for which the ratio was about 2:1). NMR spectra of cyclobutanones obtained were identical with those given above.

(*E*)-5,5-Difluoro-4-(1-hydroxycyclopropyl)-3-penten-2-one (24a): Yield 48% (66 mg), yellowish oil, eluent: hexane/ether (1:1), R_f = 0.34. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.12 (m, 4 H, CH_2CH_2), 2.31 (s, 3 H, Me), 2.52 (br. s, 1 H, OH), 6.67 (br. s, 1 H, =CH), 7.17 (t, J = 54.0 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 15.7 (s, CH_2CH_2), 31.7 (s, Me), 55.0 (s, C−OH), 111.3 (t, $^1J_{CF}$ = 237.0 Hz, CHF_2), 129.8 (t, $^3J_{CF}$ = 7.9, C-3), 147.5 (t, $^2J_{CF}$ = 20.9 Hz, C-2), 197.8 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −117.3 (br. d, $J_{H,F}$ = 54.0 Hz, CHF_2) ppm. IR (CCl_4): $\tilde{\nu}$ = 3602 w, 3300−3500 (OH), 1697 (C=O) cm^{-1}. EIMS (70 eV): *m/z* (%) = 177 (1) $[M + H]^+$, 123 (3), 83 (8), 68 (5), 55 (9), 43 (100). $C_8H_{10}F_2O_2$ (176.2): calcd. C 54.55, H 5.72; found C 54.76, H 5.78.

(*E*)-1-Cyclopropyl-4,4-difluoro-3-(1-hydroxycyclopropyl)-2-buten-1-one (25a): Yield 47% (57 mg), yellowish oil, eluent: hexane/ether (1:1), R_f = 0.34. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.12 (m, 8 H, all CH_2 of cyclopropyl) 2.22 (m, 1 H, CH of cyclopropyl), 2.55 (br. s, 1 H, OH), 6.86 (br. s, 1 H, =CH), 7.12 (t, J = 54.3 Hz, 1 H, CHF_2) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 12.6 (s, CH_2 of cyclopropyl at C-4), 15.8 (s, CH_2 of cyclopropyl at C-2), 22.8 (s, CH), 55.2 (s, C−OH), 111.8 (t, $^1J_{CF}$ = 237.0 Hz, C-1), 130.5 (t, $^3J_{CF}$ = 8.1, C-3), 146.7 (t, $^2J_{CF}$ = 21.0, C-2), 200.5 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −117.1 (br. d, J_{HF} = 54.3 Hz, CHF_2) ppm. IR (CCl_4): $\tilde{\nu}$ = 3602 w, 3300−3500 (OH), 1678 (C=O) cm^{-1}. EIMS (70 eV): *m/z* (%) = 202 (6) $[M]^+$, 187 (10) $[M - Me]^+$, 171 (21), 133 (63), 113 (57), 85 (28), 77 (18), 69 (95), 55 (35), 41 (100). $C_{10}H_{12}F_2O_2$ (202.2): calcd. C 59.40, H 5.98; found C 59.24, H 5.87.

(*E*)-1-Cyclopropyl)-4,4,4-trifluoro-3-(1-hydroxycyclopropyl-2-buten-1-one (25b): Yield **34**% (40 mg), yellowish oil, eluent: heptane/ether (1:1), R_f = 0.25. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.05−2.07 (m, 9 H, all H in cyclopropane fragments), 2.16 (br. s, 1 H, OH), 6.60 (s, 1 H, =CH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 12.3 (s, CH_2 of cyclopropyl at C-4), 14.2 (s, CH_2 of cyclopropyl at C-2), 21.7 (q, $^3J_{CF}$ = 2.1 Hz, CH), 54.7 (q, $^4J_{CF}$ = 2.1 Hz, C−OH), 122.8 (q, $^1J_{CF}$ = 277.0 Hz, C-1), 134.9 (q, $^3J_{CF}$ = 3.5, C-3), 135.4 (q, $^2J_{CF}$ = 29.4, C-2), 202.8 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −58.9 (br. s, CF_3) ppm. IR (CCl_4): $\tilde{\nu}$ = 3603 w, 3300−3500 (OH) 1692 (C=O) cm^{-1}. EIMS (70 eV): *m/z* (%) = 221 (15) $[M + H]^+$, 203 (20) $[M - OH]^+$, 131 (10), 103 (19), 69 (100), 41 (60). $C_{10}H_{11}F_3O_2$ (220.2): calcd. C 54.55, H 5.04; found C 54.36, H 5.00.

(*E*)-4,4-Difluoro-1-(1,3-dimethyl-1*H*-pyrazol-4-yl)-3-(1-hydroxycyclopropyl)-2-buten-1-one (26a): Yield 49% (69 mg), pink solid, m.p. 51−53°C, eluent: ether, R_f = 0.2. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.20 (m, 4 H, CH_2CH_2), 2.06 (br. s, 1 H, OH), 2.48 (s, 3 H, Me), 3.85 (s, 3 H, NMe), 7.00 (dd, J = 1.6, 0.7 Hz, 1 H, =CH), 7.14 (br. t, J = 54.2 Hz, 1 H, CHF_2), 7.83 (s, 1 H, 5′-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.9 (s, Me), 15.9 (br. s, CH_2CH_2), 38.9 (s, Me), 55.0 (br. s, C−OH), 112.0 (t, $^1J_{C,F}$ = 237.0 Hz, CHF_2), 121.0 (s, C-4′), 129.6 (t, $^3J_{C,F}$ = 7.8 Hz, C-3), 134.5 (s, C-5′), 147.3 (t, $^2J_{C,F}$ = 20.9 Hz, C-2), 151.8 (s, C-3′), 184.2 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F, 25 °C): δ = −116.6 (br. d, $J_{H,F}$ = 54.3 Hz) ppm. IR (CCl_4): $\tilde{\nu}$ = 3603 w, 3300−3500 (OH), 1731 (C=O) cm^{-1}. EIMS (70 eV): *m*/*z* (%) = 256 (1) $[M]^+$, 217 (2) $[M - HF - F]^+$, 149 (21), 135 (65), 123 (100), 109 (15), 93 (20), 81 (21), 69 (21), 55 (40), 41 (50). $C_{12}H_{14}F_2N_2O_2$ (256.2): calcd. C 56.25, H 5.51, N 10.93; found C 56.11, H 5.40, N 10.84.

(*E*)-1-(1,3-Dimethyl-1*H*-pyrazol-4-yl)-4,4,4-trifluoro-3-(1-hydroxycyclopropyl)-2-buten-1-one (26b): Yield 48% (50 mg), pink solid, m.p. 52−54°C, eluent: ether, R_f = 0.24. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.08 (M, 4 H, CH_2CH_2), 2.10 (br. s, 1 H, OH), 2.48 (s, 3 H, Me), 3.85 (s, 3 H, NMe), 6.73 (br. s, 1 H, =CH), 7.78 (s, 1 H, 5′-H) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 14.0 (br. s, Me), 14.6 (br. s, CH_2CH_2), 39.2 (br. s, Me), 55.3 (s, C−OH), 119.8 (s, C-4), 123.1 (q, $^1J_{C,F}$ = 277.0 Hz, CF_3), 134.5 (q, $^3J_{C,F}$ = 3.4 Hz, C-3), 135.0 (q, $^2J_{C,F}$ = 28.4 Hz, C-2), 135.5 (s, C-5′), 151.3 (s, C-3′), 185.7 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −59.0 (br. s, CF_3) ppm. IR (CCl_4): $\tilde{\nu}$ = 3603 w, 3300−3500 (OH), 1663 (C=O) cm^{-1}. EIMS (70 eV): *m*/*z* (%) = 274 (1) $[M]^+$, 245 (1) $[M - CHO]^+$, 138 (32), 123 (100), 83 (98), 66 (10). $C_{12}H_{13}F_3N_2O_2$ (274.2): calcd. C 52.56, H 4.78, N 10.22; found C 52.44, H 4.71, N 10.37.

(*E*)-1-(1-Adamantyl)-4,4-difluoro-3-(1-hydroxycyclopropyl)-2-buten-1-one (27a): Yield 49% (73 mg), Colourless solid, m.p. 68−69°C, eluent: heptane/ether (1:1), R_f = 0.4. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.11 (m, 4 H, CH_2CH_2), 1.75 (m, 12 H, Ad), 2.07 (m, 3 H, Ad), 2.5 (br. s, 1 H, OH), 6.92 (br. t, J = 54.5 Hz, 1 H, CHF_2), 6.94 (dd, J = 1.8, 0.5 Hz, 1 H, =CH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 15.7 (s, CH_2CH_2), 27.9, 36.5, 38.0 and 46.7 (all s, Ad), 55.4 (br. s, C−OH), 112.2 (t, $^1J_{C,F}$ = 237.0 Hz, CHF_2), 127.6 (t, $^3J_{C,F}$ = 8.2 Hz, C-3), 147.4 (t, $^2J_{C,F}$ = 20.3 Hz, C-2), 206.0 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −116.4 (br. d, $J_{H,F}$ = 54.5 Hz, CHF_2) ppm. IR (CCl_4): $\tilde{\nu}$ = 3603 w, 3300−3500 (OH), 1674 (C=O) cm^{-1}. EIMS (70 eV): *m*/*z* (%) = 295 (1) $[M - H]^+$, 279 (2) $[M - OH]^+$, 265 (53), 239 (11), 239 (11), 135 (62), 93 (15), 79 (20), 67 (12), 58 (23), 43 (100). $C_{17}H_{22}F_2O_2$ (296.4): calcd. C 68.90, H 7.48; found C 69.09, H 7.56.

(*E*)-1-(1-Adamantyl)-4,4,4-trifluoro-3-(1-hydroxycyclopropyl)-2-buten-1-one (27b): Yield 48% (45 mg), colourless solid, m.p. 73−76°C, eluent: heptane/ether (1:1), R_f = 0.43. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.98−1.08 (m, 4 H, CH_2CH_2), 1.76 (m, 12 H, Ad), 2.07 (m, 3 H, Ad), 3.15 (br. s., 1 H, OH), 6.75 (s, 1 H, =CH) ppm. ^{13}C NMR (50.3 MHz, $CDCl_3$, 25 °C): δ = 14.3 (s, CH_2CH_2), 27.8, 36.4, 38.4 and 46.5 (all s, Ad), 55.3 (s, C−OH), 122.7 (q, $^1J_{CF}$ = 277.0 Hz, CF_3), 134.1 (q, $^3J_{CF}$ = 3.5 Hz, C-3), 134.9 (q, $^2J_{CF}$ = 29.1 Hz, C-2), 208.0 (s, CO) ppm. ^{19}F NMR (188.3 MHz, $CDCl_3$, CCl_3F): δ = −59.2 (br. s, CF_3) ppm. IR (CCl_4): $\tilde{\nu}$ = 3606 w, 3300−3500 (OH), 1698 (C=O) cm^{-1}. EIMS (70 eV): *m*/*z* (%) = 314 (1) $[M]^+$, 297 (4) $[M - OH]^+$, 286 (2) $[M - CO]^+$, 283 (10), 245 (11), 163 (14), 135 (95), 127 (9), 123 (10), 107 (47), 95 (11), 94 (15), 93 (85), 81 (55), 79 (100). $C_{17}H_{21}F_3O_2$ (314.3): calcd. C 64.96, H 6.73; found C 65.12, H 6.79.

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