# α-Pentafluoropropionylation of Ketones and Aldehydes Using Hexafluoropropene Oxide. A Facile Synthesis of Fluorinated 1,3-Diketones

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**Synopsis.** Hexafluoropropene oxide reacts smoothly with morpholine enamines from ketones and aldehydes at 0 °C to room temperature in anhydrous THF to give pentafluorinated 1,3-diketones in good yields. The keto-enol equilibrium in the products is generally in favor of their enol form.

Fluorinated 1,3-dicarbonyl compounds have proved to be of much value as intermediates in a variety of organic transformations and as extracting agents in inorganic syntheses.[1] Two types of methods have hitherto been used for preparing these compounds; (i) the base-promoted condensation of an ester with a ketone or an aldehyde, and (ii) the Lewis acid-catalyzed acylation of a fluorine-containing ketone with an acid anhydride. These reactions are, however, often accompanied by side reactions[1a,b,2] such as self-condensation or cleavage reaction, resulting in reduced yields of the desired fluorinated 1,3-dicarbonyl compounds. In our continuing studies to extend the utilities of hexafluoropropene and its oxide to organic syntheses, we have now found that hexafluoropropene oxide (HFPO) reacts smoothly with enamines from ketones and aldehydes under mild, neutral conditions.

This paper describes the α-pentafluoropropionylation of ketones and aldehydes using HFPO, which provides a convenient method for the synthesis of fluorinated 1,3-diketones.

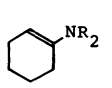
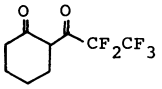
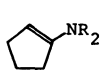
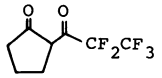
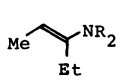
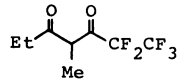
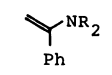
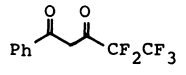
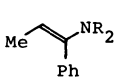
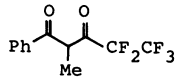
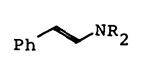
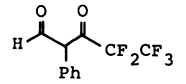
## Results and Discussion

In the present study the morpholine enamines from ketones and aldehydes were chosen as the starting enamine. The reaction of the enamines with HFPO took place exothermically, requiring the use of a solvent. Among the solvents examined, freshly distilled, anhydrous THF gave the best results. The reactions cleanly proceeded under the conditions described in the Experimental to afford the corresponding pentafluoro 1,3-diketones (**1**—**6**) in good yields. Table 1 summarizes the results of the reactions, together with the keto : enol ratios in the products. The use of anhydrous ether as solvent strikingly decreased the yields of the products. Thus, the reactions of the morpholine enamines from cyclohexanone, 3-pentanone, and acetophenone with HFPO in ether gave the corresponding 1,3-diketones in yields of no more than 25%. These results must be due to much less solubility of HFPO in ether than in THF.[3]

The IR and $^1$H NMR analyses of the pentafluoropropionylated compounds (**1**—**6**) thus obtained revealed that, except for **5**, they possess an extremely high enolic character. The keto : enol ratios, listed in Table 1, were determined by comparing the integrated intensity of the vinylic hydrogen or of the enolic hydrogen in the enol form with that of the α-methylene or methyl group in the keto form (Table 2). Compounds **1**, **2**, **4**, and **6** exist nearly exclusively as enols and compound **3** exists as a nearly equimolar mixture of the two tautomers, whereas **5** exhibits only the keto character.

To be noted is that the resonance peaks due to the enolic hydrogens are sharp (half-height width *ca.* 3—6 Hz) and appear at very low fields, *i.e.*, at 13—17 ppm, as shown in Table 2. These absorptions can be inter-

Table 1. Preparation of fluorinated 1,3-diketones

| Enamine[a] | Product | | Yield/% (keto : enol ratio)[b] |
|---|---|---|---|
|  |  | (**1**) | 80 (0 : 100) |
|  |  | (**2**) | 69 (0 : 100) |
|  |  | (**3**) | 66 (50 : 50) |
|  |  | (**4**) | 73 (0 : 100) |
|  |  | (**5**) | 74 (100 : 0) |
|  |  | (**6**) | 71 (0 : 100) |

a) The $NR_2$ denotes the morpholino group. b) Determined by $^1$H NMR analyses in $CCl_4$ solutions (15%).

Table 2. $^1$H NMR parameters of the products

| Compd | Chemical shifts and *J*/Hz |
|---|---|
| **1** | 1.7 (m, 4H), 2.5 (m, 4H), 15.29 (s, 1H) |
| **2** | 2.0 (m, 2H), 2.4 (m, 2H), 2.8 (m, 2H), 13.26 (s, 1H) |
| **3** | 1.15 (t, 3H, 7.5), 1.94 (t, 3H, 2.9), 2.56 (q, 2H, 7.5), 16.10 (t, 1H, 1.8)<br>1.06 (t, 3H, 7.5), 1.34 (d, 3H, 6.9), 2.48 (q, 2H, 7.5), 4.01 (q, 1H, 6.9) |
| **4** | 6.55 (s, 1H), 7.5 (m, 3H), 7.9 (m, 2H), 15.24 (s, 1H) |
| **5** | 1.48 (d, 3H, 7.2), 4.88 (q, 1H, 7.2), 7.7 (m, 5H) |
| **6** | 7.3 (m, 5H), 8.20 (s, 1H), 14.37 (s, 1H) |

preted as characteristic of 1,3-dicarbonyl compounds containing electron-withdrawing substituent groups, on the basis of the generalization suggested by Lintvedt and Holtzclaw[4] and of the observations made by Engel and Chappelow.[5]

The strong and broad absorptions in the regions of 1690—1560 and 3500—2200 $cm^{-1}$ in the IR spectra of these fluoro 1,3-diketones also reveal the presence of the intramolecularly hydrogen-bonded enolic structure. The former absorption can be ascribed to the conjugate chelation[6] of the keto groups in the molecule.

In the reactions of the morpholine enamines from acetophenone, propiophenone, and phenylacetaldehyde with HFPO, pentafluoropropionylated enamines[7] were obtained when the reaction was quenched with a 5% $NaHCO_3$ aqueous solution, instead of an acid. Successive acid treatment of them gave the corresponding 1,3-diketones (**4**—**6**). These facts strongly suggest that the initial step of the reaction is the isomerization of HFPO[8] to pentafluoropropionyl fluoride by an enamine, followed by the acylation of the enamine with the acid fluoride to give the products.

## Experimental

Infrared spectra were recorded with a Shimadzu IR-400 infrared spectrometer. A Varian EM-390 spectrometer was used to measure $^1H$ and $^{19}F$ NMR spectra, in solutions of $CCl_4$ with internal $Me_4Si$ and external trifluoroacetic acid as a reference, respectively. Mass spectra were obtained with a Hitachi RMS-4 spectrometer.

The morpholine enamines from ketones and aldehydes were prepared according to the literature procedure.[9]

*General Procedure for the Reaction of HFPO with Morpholine Enamines.* Into a stirred solution of a morpholine enamine (25 mmol) in anhydrous THF (25 ml), which had been cooled to −20 to −15 °C, was introduced HFPO (16 mmol) under nitrogen at such a rate that the reaction temperature should not rise over 0 °C. After the introduction of HFPO was over, the whole mixture was stirred at room temperature for 20 h. In the case of the morpholine enamine from 3-pentanone, the temperature was maintained at −50 to −40 °C for 10 h and then at room temperature for 10 h. To the mixture was added 5% HCl (20 ml) dropwise under cooling with an ice–water bath. After stirred at room temperature for 2 h, the reaction mixture was poured into water (70 ml). The organic layer was separated and the aqueous layer was extracted with ether. The combined extracts were washed with water, dried ($Na_2SO_4$), and concentrated under reduced pressure. The residual oil was chromatographed on silica gel with hexane or benzene and, if necessary, the product was distilled *in vacuo* to give a pure 1,3-diketone.

When the reaction was quenched with a 5% $NaHCO_3$ aqueous solution, β-pentafluoropropionylated morpholine enamines were obtained as the product.

*2-(Pentafluoropropionyl)cyclohexanone (**1**)*: Bp 77—78 °C/20 mmHg (1 mmHg=133.3 Pa) (lit,[10] bp 104.5 °C/42 mmHg); IR (film) 3300—2400, 1620—1560, 1260—1100, 1036, 922, 725 $cm^{-1}$; $^{19}F$ NMR δ −3.34 (s, 3F), −39.86 (s, 2F); MS *m/e* (%) 244 ($M^+$, 35), 125 (100).

*2-(Pentafluoropropionyl)cyclopentanone (**2**)*: Bp 83—84 °C/35 mmHg (lit,[10] bp 82 °C/30 mmHg); IR (film) 3400—2250, 1690, 1633, 1330, 1288, 1205, 1098, 1029, 1016, 815, 744 $cm^{-1}$; $^{19}F$ NMR δ −4.65 (t, $J$=1.7 Hz, 3F), −43.08 (q, $J$=1.7 Hz, 2F); MS *m/e* (%) 230 ($M^+$, 42), 111 (100).

*1,1,1,2,2-Pentafluoro-4-methyl-3,5-heptanedione (**3**)*: Bp 82—84 °C/54 mmHg; IR (film) 3500—2300, 1758, 1717, 1632, 1328, 1200, 1120, 1084, 1072, 972 $cm^{-1}$; $^{19}F$ NMR δ −3.35 (s, 3F), −43.60 and −43.70 (two s, 2F) for the keto form, −3.95 (t, $J$=1.7 Hz, 3F), −38.02 (m, 2F) for the enol form; MS *m/e* (%) 232 ($M^+$, 4), 57 (100).

Found: C, 41.60; H, 3.78%. Calcd for $C_8H_9F_5O_2$: C, 41.39; H, 3.91%.

*4,4,5,5,5-Pentafluoro-1-phenyl-1,3-pentanedione (**4**)*: Bp 75.5—76.5 °C/4 mmHg (lit,[10] bp 128.5 °C/28 mmHg); IR (film) 3200—2300, 1606, 1576, 1330, 1203, 1126, 1028, 1010, 998, 768, 690 $cm^{-1}$; $^{19}F$ NMR δ −4.05 (s, 3F), −45.00 (s, 2F); MS *m/e* (%) 266 ($M^+$, 43), 69 (100).

*4,4,5,5,5-Pentafluoro-2-methyl-1-phenyl-1,3-pentanedione (**5**)*: Bp 75—75.5 °C/1 mmHg; IR (film) 1762, 1682, 1452, 1335, 1278, 1210, 1110, 970, 718, 704 $cm^{-1}$; $^{19}F$ NMR δ −3.63 (s, 3F), −43.30 and −43.57 (two s, 2F); MS *m/e* (%) 280 ($M^+$, 2), 105 (100).

Found: C, 51.32; H, 3.11%. Calcd for $C_{12}H_9F_5O_2$: C, 51.44; H, 3.24%.

*4,4,5,5,5-Pentafluoro-2-phenyl-1,3-pentanedione (**6**)*: Mp 73.5—74.5 °C; IR (KBr) 3500—2300, 1608, 1592, 1377, 1230, 1183, 1133, 1119, 1035, 1020, 830, 716 $cm^{-1}$; $^{19}F$ NMR δ −3.17 (s, 3F), −37.53 (s, 2F).

Found: C, 49.77; H, 2.54%. Calcd for $C_{11}H_7F_5O_2$: C, 49.63; H, 2.65%.

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