Annelation of Enamines with 1-Fluorovinyl Methyl Ketone

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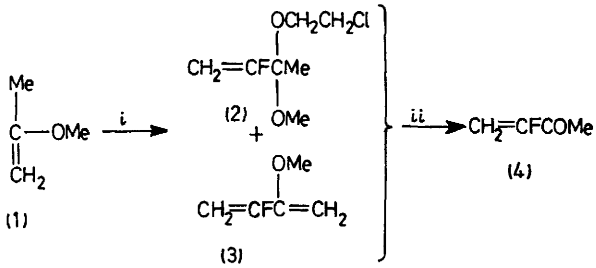
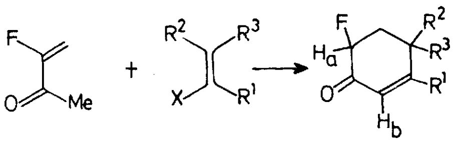
Summary On condensation of enamines with 1-fluorovinyl methyl ketone, obtained by condensation of dichlorofluoromethane with 2-methoxypropene, fluorinating annelation takes place giving 6-fluorocyclohexenones.

1-FLUOROVINYL METHYL KETONE (FVMK) is easily polymerized,[1] but we found that it could be stabilised by a small percentage of hydroquinone and used for annelation of enamines, providing a straightforward route to fluorinated cyclohexenones. The reagent (**4**) [b.p. 71°C; λ_{max} (cyclohexane) 218 nm (ϵ 8050); ν_{max} (CCl_4) 1640 and 1720 cm^{-1}; ϕ (CCl_4; $CFCl_3$ reference) 115 p.p.m.; δ 2·26 (Me), 4·8 (H *cis* to F), and 5·33 (*trans*-H); ^3J (FH_{trans}) 43·5, ^3J(FH_{cis}) 17·5, ^2J(HH) 3·6, and ^4J(FH) 2·4 Hz] was prepared by a modification of Buddrus's method[2] in 45% overall yield (Scheme 1).



SCHEME 1. Reagents: i, ethylene oxide, $CHFCl_2$, Et_4NBr; 150 °C; ii, H^+.

The experimental procedure described for methyl vinyl ketone[3] (without solvent) was used for the condensation of $\beta\beta$-disubstituted enamines with FVMK. 2-Methyl-1-pyrrolidinopropene (**5a**) was mixed with FVMK (2 equiv.) at room temperature and after 12 h, 6-fluoro-4,4-dimethylcyclohexanone (**6a**) was obtained [65% yield, m.p. 65 °C (from pentane); λ_{max} (cyclohexane) 218 nm (ϵ 13,600); ν_{max} ($CHCl_3$) 1610 and 1705 cm^{-1}; ϕ ($CDCl_3$) 191 p.p.m.; δ 1·23 and 1·26 (Me), 5·0 (H_a), 5·76 (H_b), and 6·63 (H_c); ^2J (H_aF) 48, ^3J (HF) 9·15, ^3J (H_bH_c) 9·75, and ^4J(H_bF) 4·4 Hz] (Scheme 2).

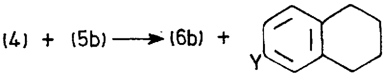


(4) (5) (6)

a: $R^1{=}H_c$, $R^2{=}R^3{=}Me$
b; $R^1,R^3{=}[CH_2]_4$,$R^2{=}H$
c; $R^1{=}H_c$, $R^2{=}H$, $R^3{=}Pr^i$

Scheme 2. For (**5a**) X = pyrrolidino, for (**5b**) X = morpholino or Me_2N, and for (**5c**) X = piperidino.

It was more difficult to follow the usual experimental procedures (without solvent,[3] or in boiling dioxan[4] or benzene[5]) in the condensation of β-monosubstituted enamines and especially cyclic enamines, since large amounts of aromatic side products were formed. *E.g.* treatment of 1-morpholinocyclohexene (**5b**) with FVMK produced a mixture of (**6b**) and an aromatic compound (**7**) (Y = morpholino in benzene; Y = OH in dioxan or without solvent) (Scheme 3). This aromatisation, probably due to enolisation or dienamine formation[5] followed by loss of HF, was avoided by using 1-dimethylaminocyclohexene instead of (**5b**) and diethyl ether as solvent; the dimethylamine was removed slowly with part of the solvent using a short spinning band distillation apparatus. After hydrolysis, we obtained 3-fluoro-$\Delta^{1,9}$-octalin-2-one (**6b**) [45% yield, b.p. 132 °C at 0·5 mmHg].



(7)

Scheme 3

With some β-monosubstituted enamines, *e.g.* with 1-piperidino-3-methylbutene (**5c**), the condensation could be carried out without solvent since the proportion of aromatic product analogous to (**7**) was only *ca.* 15%; 6-fluoro-4-isopropylcyclohexenone (**6c**) was obtained in 30% yield.

The fluorinating annelation was also performed with 3,7-dimethyl-1-piperidino-octa-1,6-diene.

This method constitutes a safe preparation of fluorinated cyclohexenones which until now used perchloryl fluoride.[6]

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