SULFENYLATION OF CYCLOHEXENONE ESTERS BY TRIFLUOROMETHANE-SULFENYL CHLORIDE

Wanda ZANKOWSKA-JASINSKA, Barbara ZALESKA

Department of Organic Chemistry, Jagiellonian University

30-060 Cracow (Poland)

Alois HAAS

Chair of Inorganic Chemistry II, Ruhr-University,

4630 Bochum (F.R.G.)

SUMMARY

The reactions of ethyl 2-methyl-4-oxo-2-cyclohexene carboxylate 1 and ethyl 4-methyl-2-oxo-4-cyclohexene carboxylate 4 with CF_3SCl have been studied. It has been shown by ^1H-, ^{13}C- and ^{19}F-NMR-studies that in the case of 1 substitution by the SCF_3 takes place mainly at the 3-position. Substitution has also been observed for its ß-isomer 4.

INTRODUCTION

The present work was undertaken to investigate the reaction between ethyl 2-methyl-4-oxo-2-cyclohexene carboxylate 1, its ß-isomer 4 and trifluoromethylsulfenyl chloride.

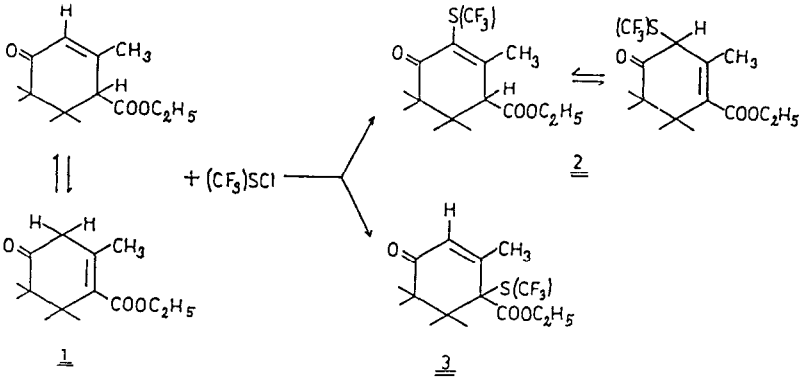
RESULTS

The only previously known [1] alkylation of 1 leads to the C-3 and C-1 alkylation products, in a proportion depending on the nature of the alkylating agents.

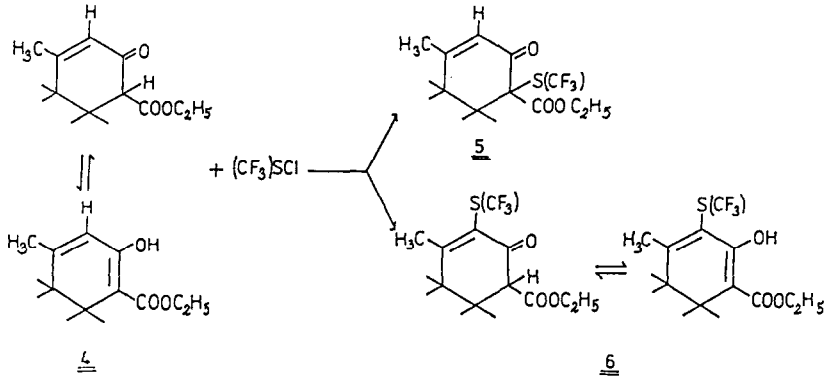
Direct treatment of 1 with equimolar amounts of CF_3SCl at 0°C (15 h) in dry n-pentane solution yields mainly 2 and minor amounts of 3 as shown below: Scheme 1

Under the same conditions the reaction of 4 with trifluoromethanesulfenyl chloride gives rise to formation of 5 and small amounts of 6 according to Scheme 2.

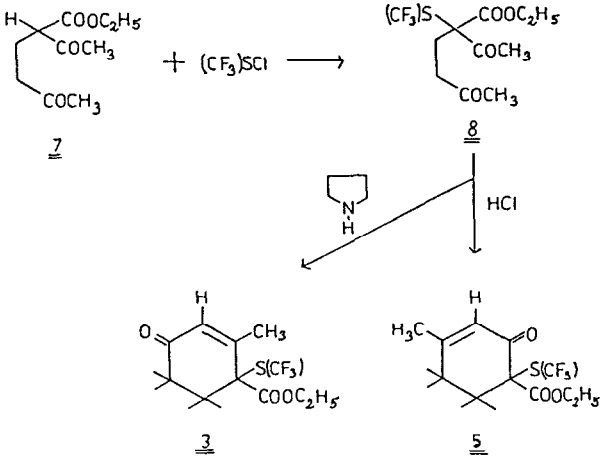
0022-1139/84/$3.00



Scheme 1



Scheme 2



Scheme 3

Compounds 3 and 5 were also prepared by the following route: Base catalysed Michael addition [2] of ethyl ester of acetoacetic acid to methyl vinyl ketone gives 7. The reaction of trifluoromethane-sulfenyl chloride with ethyl 2-acetyl-5-oxo-hexanoate 7 in dry n-pentane solution leads to substitution product 8. In general 8 can undergo aldol cyclisation [3] in two ways giving either 3 or its structural isomer 5.

Regioselective cyclisation of 7 catalysed by pyrrolidinium acetate leads to 3. The same reaction but catalysed by hydrogen chloride gives 5 according to Scheme 3.

The constitution of the isomers were elucidated by means of ^{1}H-, ^{19}F- and partly ^{13}C-NMR-spectroscopy. The ^{1}H-NMR-spectrum of 2 shows δ(1-CH) at 3.6 ppm splitting to a triplet by the CH_2 group in the 6-position with J = 4-5 Hz and no vinyl proton characteristic of 1. The ^{1}H-NMR-spectrum of 3 differs from that of 2 in the disappearance of δ(1-CH) and in the appearence of δ(3-CH) at 6.05 ppm as a singlet. The same arguements stand for the constitutions of 5 and 6.

The ^{19}F-NMR-spectrum of 3 and 5 which have the CF_3S-group in position 1 show $\delta(CF_3S)$ at 36.6 and 36.0 ppm while 2 and 6 with CF_3S in 3-position exhibit $\delta(CF_3S)$ at 40.3 and 41.2 ppm. The vinyl carbons of 2 resonate at δ = 128.3 and 127.4 ppm. Off-resonance decoupling reveals the nature of these vinyl carbons showing singlets whereas 3 gives a doublet. The off-resonance decoupling of the ^{13}C-NMR-spectra shows a singlet for 5 at δ(1-C) = 49.7 ppm and a doublet at 45.8 ppm for 6.

It is known that ß-and γ-keto esters of cyclohexenone derivatives have two acid hydrogens of different activity in positions 1 and 3. The reaction of CF_3SCl with 1 and 4 always gave two monosubstituted derivatives in position 1 and 3, but in different amounts. The quantitative ratio of both products gives information on the relative acidity of the products. In case of delta-ketoester 1 the proton at C-3 is more acidic and in the beta-ketoester 4 the proton at C-1, both activated by a neighbouring ketocarbonyl group, has the greater acidity.

EXPERIMENTAL

IR spectra were recorded as capillary films of neat liquids between KBr plates on a Perkin Elmer grating spectrometer 125. Weak bands and shoulders are not given. ^{1}H- and ^{19}F-NMR: Bruker HX 60. ^{19}F- and ^{1}H-NMR spectra were taken as solutions in C_6F_6 containing TMS. ^{19}F-chemical shifts are converted to CCl_3F. ^{13}C-NMR: Bruker WH 90, $CDCl_3$ as solvent and internal standard, $\delta(^{13}C)$ values are converted to TMS.

Ethyl 2-methyl-3-trifluoromethylsulfenyl-4-oxo-2-cyclohexene carboxylate 2 and ethyl 2-methyl-1-trifluoromethylsulfenyl-4-oxo-2-cyclohexene carboxylate 3

To a solution of 9 g (0.05 mole) 1 in 50 ml anhydrous n-pentane 6.5 g (0.05 mole) CF_3SCl were condensed. The mixture was stirred at 0°C 815 h) and the solvent removed. The residue, a red oil, was purified by fractional destillation giving 6.0 g (41%) 2 and 1.1 g (8%) 3, a pale yellow oil.
2: $C_{11}H_{13}F_3O_3S$ (282.2), MS: M^+ 282 (7%).
Boiling point 132°C/0.2 Torr.; IR: 2990-2880 (m, br), 1730 (s), 1690 (s), 1630 (m), 1590 (m), 1190 (s), 1160 (s), 1110 (s), 760 (m) cm^{-1}.
^{1}H-NMR: $\delta(\underline{CH_3}\text{-}CH_2) = 1.3$ (tr), $\delta(\underline{CH_2}\text{-}CH_3) = 4.2$ (qu), $J(CH_3\text{-}CH_2) = 7$ Hz; δ(1-CH) = 3.6 (tr); J(CH-6-CH_2) = 4-5 Hz; $\delta(2\text{-}CH_3) = 2.45$ (s); $\delta(CH_2\text{-}CH_2) = 2.5\text{-}2.2$ (m) ppm. Signals of vinyl protons characteristic for 1 were not observed.
^{13}C-NMR: $\delta(CF_3) = 131.7$ (qu), δ(vinyl-C) = 128.3 and 127.4 ppm. The off resonance decoupling reveals the nature of these vinyl carbons, showing singles: 3 appears at 124.4 ppm as a doublet.
^{19}F-NMR: $\delta(CF_3) = -40.3$ ppm.
3: $C_{11}H_{13}F_3OS$ (282.2), MS: M^+, 282 (30%). Analyses: Calc.: C 46.81 H 4.61; S 11.34; Found: C 46.6; H 4.5; S 11.2.
Boiling point 124°C/0.2 Torr., IF: 2980-2880 (m, br), 1720 (s), 1680 (s), 1590 (s), 1160 (s), 1110 (s), 780 (m), 760 (m) cm^{-1}.
^{1}H-NMR: $\delta(\underline{CH_3}\text{-}CH_2) = 1.35$ (tr), $\delta(\underline{CH_2}\text{-}CH_3) = 4.25$ (qu); $J(CH_3\text{-}CH_2) = 1$ Hz; $\delta(2\text{-}CH_3) = 2.15$ (s), $\delta(CH_2\text{-}CH_2) = 2.45\text{-}2.3$ (m), δ(3-HC) = 6.05 (s) ppm.
^{19}F-NMR: $\delta(CF_3) = 36.6$ ppm, ^{13}C-NMR: δ(vinyl-C) = 124.4 (d) ppm.

Ethyl 4-methyl-1-trifluoromethylsulfenyl-2-oxo-3-cyclohexene carboxylate 5 and ethyl 4-methyl-3-trifluoromethylsulfenyl-2-oxo-3-cyclohexene carboxylate 6

As described above 9 g (0.05 mole) 4 reacted with 6.5 g (0.05 mole) CF_3SCl in anhydrous n-pentane to give a brown oil, which on fractional distillation gave 5.8 g (38%) 5 and 1.5 g (12%) 6.

5: $C_{11}H_{13}F_3O_3S$ (282.2), MS: M^+, 282 (1.5%). - Analyses: Calc. C 46.81; H 4.61; S 11.34; Found: C 47.0; H 4.3; S 11.1.

Boiling point 111°C/0.2 Torr.; IR: 2980-2880 (m, br), 1745 (s), 1680 (s), 1630 (s), 1190 (s), 1160 (s), 1120 (s), 770 (m), 750 (m) cm^{-1}.

^{1}H-NMR: $\delta(\underline{CH_3}\text{-}CH_2) = 1.25$ (tr), $\delta(\underline{CH_2}\text{-}CH_3) = 4.12$ (qu), $J(CH_3\text{-}CH_2) = 7.1$ Hz, $\delta(CH_3) = 2.0$ (s), $\delta(CH_2\text{-}CH_2) = 2.0\text{-}2.4$ (m), δ(3-CH) = 6.01 (s) ppm.

^{19}F-NMR: $\delta(CF_3) = 36.0$ ppm. ^{13}C-NMR: δ(1-C) = 49.7 (s) ppm.

6: $C_{11}H_{13}F_3O_3S$ (282.2) ,MS: M^+, 282 (10.0%).

Boiling point 107°C/0.2 Torr.; IR: 2990-2900 (m, br), 1740 (s), 1700 (s), 1595 (s), 1200-1110 (s, br), 765 (m) cm^{-1}.

^{1}H-NMR: $\delta(\underline{CH_3}\text{-}CH_2) = 1.25$ (tr), $\delta(\underline{CH_2}\text{-}CH_3) = 4.2$ (qu), $J(CH_3\text{-}CH_2) = 7$ Hz. $\delta(CH_3) = 2.0$ (s), $\delta(CH_2\text{-}CH_2) = 2.6\text{-}2.4$ (m), δ(1-CH) = 3.3 (tr), $J(CH_2\text{-}CH) = 4$ Hz.

^{19}F-NMR: $\delta(CF_3) = 41.2$ ppm, ^{13}C-NMR: δ(1-C) = 45.8 (d).

Ethyl 2-acetyl-2-trifluoromethylsulfenyl-5-oxohexanoate 8

The reaction between 9.8 g (0.05 mole) 7 and 6.5 g (0.05 mole) CF_3SCl under similar conditions gave after fractional distillation 8.95 g (60 %) 8.

$C_{11}H_{15}F_3O_4S$ (298.2), MS: M^+, 298 (2.0%). - Analyses: Calc.: C 44.15; H 5.01; S 12.0; Found: C 46.81; H 4.61; S 11.34.

Boiling point 108°C/0.2 Torr.; IR: 2980-2900 (m, br), 1728 (s), 1670 (s), 1630 (s), 1180 (s), 1120 (s), 755 (m) cm^{-1}.

^{1}H-NMR: $\delta(\underline{CH_3}\text{-}CH_2) = 1.3$ (tr), $\delta(\underline{CH_2}\text{-}CH_3) = 4.3$ (qu), $J(CH_3\text{-}CH_2) = 7$ Hz. $\delta(CH_2\text{-}CH_2) = 2.6\text{-}2.4$ (m), $\delta[CH_3C(O)] = 2.2$ (s) and 2.1 (s).

^{19}F-NMR: $\delta(CF_3) = 36.6$ ppm.

Cyclisation of ethyl 2-acetyl-2-trifluoromethylsulfenyl-5-oxo-hexanoate 8 to 3 in the presence of pyrrolidine

A solution of 6 g (0.02 mole) 8 in 20 ml of a 9:1 ehtanol-water mixture containing 1 g glacial acetic acid and 1 g pyrrolidin was refluxed for 1 h. After removing the solvent the residue was treated with 0.1 m HCl and dilute $NaHCO_3$. The aqueous solution was extracted with ether, dried with Na_2SO_4 and evaporated to dryness. Fractional destillation of the residue gives 2.8 g (50%) 3 as a yellow oil.
Boiling point 132°C/0.2 Torr. Spectroscopic data are in good agreement with the sample obtained from 1.

Cyclisation of 8 to 5 in the presence of HCl

A benzene solution of 8 was saturated with HCl at 0°C. After 18 h the mixture was washed with dilute $NaHCO_3$ and separated. The solvent was removed and the residue was refluxed with $(CH_3)_2NH$ for 2 h. The mixture was taken up in ice water, acidified with sulfuric acid, and extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate, dried with Na_2SO_4 and evaporated. The residue was destilled under reduced pressure giving 3.6 g (60%) 5.
Boiling point 111°C/0.2 Torr. The product was identical with the one obtained from 4.

REFERENCES

1. D. Nasipi, K. Mitra and S. Vankataraman, J. Chem. Soc. Perkin I (1972) 1836.
2. H. Henecka, Chem. Ber. 81, 179 (1948).
3. A.L. Begbie and G.T. Golding, J. Chem. Soc. Perkin I, (1972) 602