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LEWIS ACID CATALYZED ADDITION OF 2,2,2-TRIFLUORODIAZOETHANE TO UNACTIVATED ALDEHYDES

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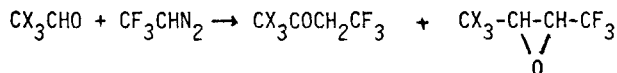
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SUMMARY

Condensations of 2,2,2-trifluorodiazooethane with pentanal, cyclohexancarboxaldehyde and benzaldehyde have been performed in presence of antimony pentachloride or boron trifluoride. These reactions lead mainly to homologated aldehydes or ketones α substituted by a trifluoromethyl group.

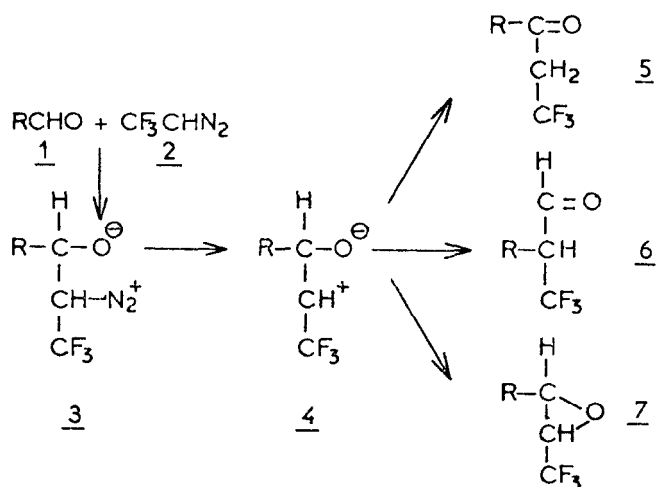
INTRODUCTION

2,2,2-trifluorodiazooethane is not a very reactive diazo compound [1]. Until now, addition to aldehydes was performed only in the case of electron withdrawing substituents on the carbonyl group [2,3]; reaction with chloral or fluoral led to a mixture of ketone and epoxyde.



X=Cl,F

We report that unactivated aldehydes are able to react with this fluorinated diazo compound provided that the reaction is performed in presence of Lewis acids [4]. This condensation leads mainly to homologated ketones 5 and aldehydes 6 α substituted by a trifluoromethyl group (scheme 1).



R=butyl (a) , cyclohexyl (b) , phenyl (c)

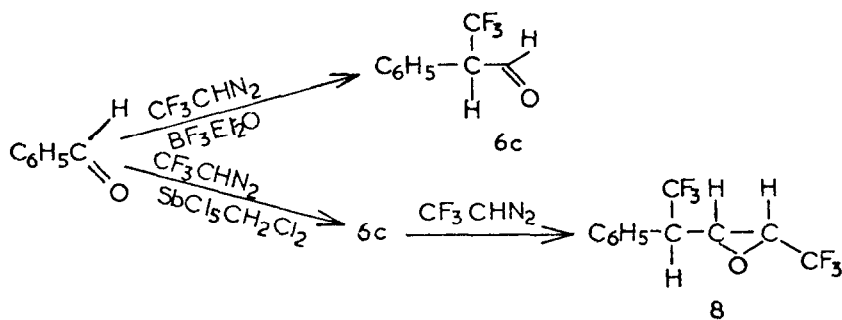
Scheme 1

Ketone 5 can be formed from the intermediate 4 by an hydrogen migration. Aldehyde 6 can be produced from 4 by a migration of an alkyl or aryl group. This observation is rather unusual ; in the case of the condensation of aldehydes with diazomethane hydrogen migrates in preference to alkyl [5]. Epoxyde 7 detected in very small amounts, results of the ring closure of the intermediate 4.

The catalytic activity of Lewis acids results probably of the increased carbonyl polarisation due to the coordination of BF_3 or SbCl_5 with the oxygen atom. Attack of the fluorinated diazo compound occurs more easily on this polarised double bond. The condensation has been performed with aldehydes bearing a linear alkyl chain (R=butyl), a ramified alkyl chain (R=cyclohexyl) and an aromatic nucleus (R=phenyl).

The ketone 5a has been obtained from pentanal in methylene chloride at -70°C in presence of SbCl_5 . Aldehyde 6b and ketone 5b are produced in a ratio 1-1, from cyclohexancarboxaldehyde in presence of BF_3 in ether at 0°C .

In the same conditions, benzaldehyde leads to the aldehyde 6c. However, in presence of SbCl_5 in methylene chloride at -70°C , the reaction goes further until the formation of the epoxyde 8 (scheme 2).



Scheme 2

From all the results, it appears that SbCl_5 in methylene chloride behaves like a stronger Lewis acid than BF_3 in ether, and that the migration aptitude in the intermediate 4 follows the order :

phenyl > hydrogen, cyclohexyl > butyl.

The activation of simple aldehydes by Lewis acid catalysts allows the preparation of various α trifluoromethyl carbonyl compounds [6] from the easily available 2,2,2-trifluorodiazooethane [7].

EXPERIMENTAL

^1H and ^{19}F nmr spectra were recorded on a Jeol C60HL instrument. The chemical shift values δ are expressed in ppm relative to Me_4Si (for ^1H nmr spectra) or CFCl_3 (for ^{19}F nmr spectra) as internal standards. Spectra at 90 MHz were obtained with a Bruker WH90DS instrument. IR spectra were recorded with a Perkin-Elmer 167 spectrometer. Preparative glc were performed with a Varian aerograph model 920 chromatograph. Mass spectra were obtained on an A.E.I. MS30 instrument.

The 2,2,2-trifluorodiazooethane pure or in ether solution has been prepared according to Gilman and Jones [7].

WARNING

Stringent safety precautions are necessary at all times [3].

Reaction with pentanal

To 1.72 g (0.02 mole) of pentanal in 25 ml of methylenechloride at -70°C are added 3 g (0.01 Mole) of antimony pentachloride. Then, 0.02 mole of 2,2,2-trifluorodiazaoethane in 20 ml of methylenechloride are added under stirring. After one hour at -70°C , the temperature is allowed to rise until 20°C . The mixture is poured into 150 ml of a saturated solution of sodium bicarbonate and filtrated on a sintered glass. The solid is washed with 150 ml of methylenechloride. The organic layers are mixed, washed with a solution of sodium bicarbonate and dried over magnesium sulfate. The solvent is removed under vacuum. The distillation of the residue gives 1.6 g of 1,1,1-trifluoro-3-heptanone 5a (nc) (52 % yield) Bp : 40° at 15 Torr ; ir (CCl_4) 1734 cm^{-1} .

^1H nmr (CDCl_3) $\delta = 2.5\text{ ppm}$ (2H) ; 3.17 ppm (2H ; q ; $J_{\text{HF}} 10.3\text{ Hz}$)
 ^{19}F nmr (CDCl_3) $\delta = 55\text{ ppm}$ (t ; $J_{\text{HF}} = 10.3\text{ Hz}$) ; ms : m/e = 168 (M) ; 126.

Reaction with cyclohexancarboxaldehyde

To 5.6 g (0.05 mole) of cyclohexancarboxaldehyde in 100 ml of diethyl ether at 0°C are added 7.25 g (0.05 mole) of boron trifluoride etherate in 20 ml of ether under stirring. Then is added in three hours a solution of approximately 0.05 mole of 2,2,2-trifluorodiazaoethane in 225 ml of ether prepared according to Gilman and Jones. After one hour more, 100 ml 2N HCl are added. The mixture is extracted with 200 ml of ether. The organic layer is washed with a solution of sodium bicarbonate and dried over magnesium sulfate. After solvent removal, the residue is distilled under 18 Torr. The fraction $50-90^{\circ}\text{C}$ (5.4 g 58 % yield) contains an equimolar quantity of two isomers which have been separated by preparative g.l.c. on a 30 % SE30 PAW 45/60 column at 150°C .

1) 3,3,3-trifluoro-2-cyclohexyl propanal 6b (nc)
 ir (CCl_4) 1735 cm^{-1}
 ^1H nmr (CDCl_3) $\delta = 9.6\text{ ppm}$ (1H ; d x q ; $J_{\text{HH}} : 3.5\text{ Hz}$ $J_{\text{HF}} : 1.7\text{ Hz}$)
 2.8 ppm (1H ; q x d x d ; $J_{\text{HF}} : 9.8\text{ Hz}$ $J_{\text{HH}} : 3.5\text{ Hz}$ $J_{\text{HH}} : 2.0\text{ Hz}$)
 ^{19}F nmr (CDCl_3) $\delta = 60\text{ ppm}$ (d large peaks ; $J_{\text{HF}} : 9.8\text{ Hz}$) ms :
 m/e = 195 (M + 1) ; 193 (M-1) 128.

2) 1,1,1-trifluoroethylcyclohexylketone 5b (nc)
 ir (CCl_4) 1720 cm^{-1}
 ^1H nmr (CDCl_3) $\delta = 3.2\text{ ppm}$ (2H ; q ; $J_{\text{HF}} : 10.1\text{ Hz}$)
 ^{19}F nmr (CDCl_3) $\delta = 60\text{ ppm}$ (t ; $J_{\text{HF}} : 10.1\text{ Hz}$) ms : m/e = 194 (M) ; 152.

Reaction with benzaldehydea) in presence of boron trifluoride

To 5.3 g (0.05 mole) of benzaldehyde in 100 ml of ether at 0° C, are added 7.25 g (0.05 mole) of boron trifluoride etherate in 20 ml of ether. Then is added in three hours a solution of 0.05 mole of trifluorodiazooethane in 225 ml of ether prepared according to Gilman and Jones. After one hour more, 100 ml 2N HCl are added. The mixture is extracted with 200 ml of ether. The organic layer is washed with a solution of sodium bicarbonate and dried over magnesium sulfate.

After solvent removal, 6.6 g of 3,3,3-trifluoro 2 phenyl propanal 5c (nc) is distilled (70 % yield). Bp 50-56 ° C at 0.5 Torr. ir (CCl₄) : 1735 cm⁻¹.

¹H nmr (CDCl₃) δ = 9.6 ppm (1H ; q x d ; J_{HF} : 2.5 Hz ; J_{HH} : 1.3 Hz)
4.1 ppm (1H ; q x d ; J_{HF} : 9.1 Hz ; J_{HH} : 1.3 Hz)

¹⁹F nmr (CDCl₃) δ = 63 ppm (d x d ; J_{HF} : 9.1 Hz ; J_{HF} : 2.5 Hz)
ms : m/e = 188 (M) 168, 160, 140.

b) in presence of antimony pentachloride

To 1.06 g (0.01 mole) of benzaldehyde in 10 ml of methylene chloride at -70°, are added 1.5 g (0.005 mole) of antimony pentachloride in 10 ml of methylene chloride. Then are added in one hour 0.02 mole of 2,2,2-trifluorodiazooethane in 20 ml of methylene chloride. After one hour more, the temperature is allowed to rise until 20° C. The mixture is poured into 100 ml of sodium bicarbonate solution and filtrated on a sintered glass. The organic layers are mixed, washed with a solution of sodium bicarbonate and dried over magnesium sulfate. The solvent is removed under vacuum. Distillation of the residue gives 1.1 g (41 % yield) of 1,1,1,5,5,5-hexafluoro-2,3-epoxy-4-phenyl pentane 8 (nc). Bp : 30-40° at 0.3 Torr.

¹H nmr (CDCl₃) δ = 3.7 ppm (1H ; d x d ; J_{HH} : 7.3 Hz ; J_{HH} : 2.0 Hz) 3.1 ppm (2H ; 90 MHz nmr spectrum shows that each hydrogen is a quatruplet of doublet, one with J_{HF} : 4.7 Hz and J_{HH} 2.0 Hz ; the other one with J_{HF} : 2.7 Hz and J_{HH} : 7.3 Hz). ¹⁹F nmr (CDCl₃) δ = 65 ppm (3F ; d ; J_{HF} : 2.7 Hz) 71 ppm (3F ; t ; J_{HF} : 4.7 Hz) ms:m/e=270(M), 201,173,159,77,69.

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