# THE ADDITION OF CYANIDE TO 1,1,1-TRIFLUOROACETONE: ONE STEP FORMATION OF A HETEROCYCLIC RING

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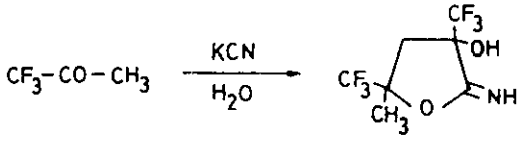
Abstract- The addition of potassium cyanide to 1,1,1-trifluoroacetone results in the one step formation of a novel iminooxolane ring.

There are only a limited number of literature references describing the use of 1,1,1-trifluoroacetone (1,1,1-TFA) in heterocyclic synthesis. Thus, the [2+2]-cycloaddition of 1,1,1-TFA to azaphospholes leads to 7-oxa-5-aza-1-phosphabicyclo-[3,2,0]-hept-2-enes.[1,2] 1,4,2-Dioxaphospholanes are obtained by reaction of trialkylphosphites with 1,1,1-TFA[3] and 2-trifluoromethylcinchonimic acids result from isatin as the starting material.[4] The photochemical cycloaddition of 1,1,1-TFA to azines has also been described, and leads to oxazol derivatives.[5] An oxetan ring is obtained from a similar cycloaddition to 1,2-difluoroethylenes.[6]

On the other hand, the autocondensation of 1,1,1-TFA in the presence of bases, such as sodium ethoxide and sodamide is also Known and affords the hydrate of 1,1,1,5,5,5-hexafluoro-2-hydroxy-2-methylpentan-4-one.[7] However, several authors[8,9] have also reported the formation of a trimer in different basic conditions, the structure of which was identified as a tetrahydropyran derivative.[10]

This paper describes the results obtained from the reaction of 1,1,1-TFA with potassium cyanide. No cyanohydrin is formed and a five-membered heterocyclic compound is obtained instead, in a one step reaction[11] (Scheme 1).

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Scheme 1

In a typical experiment, 0.02 mol of 1,1,1-trifluoroacetone was added to a solution of potassium cyanide (0.01 mol) in water (10 ml). Upon stirring, an exothermic reaction took place and a copious precipitate was formed,[13] with 69% yield. The resulting compound was purified by recrystallization in toluene or, better still, by sublimation, to get a white, crystalline product of mp 152-154°C.

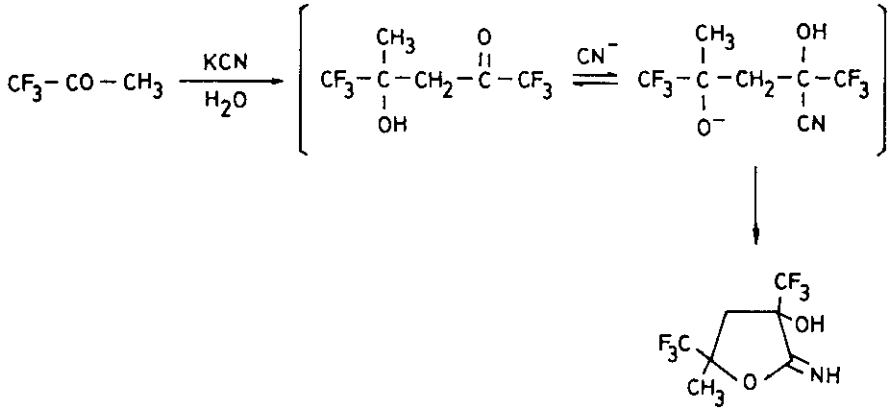
Analytical and spectral properties of this compound lead to a structure of 3-hydroxy-2-imino-5-methyl-3,5-bis(trifluoromethyl)oxolane 1.

The microanalytical and mass apectral data (C, 33.54; H, 2.31; N, 5.54; $M^+$, 251) are in agreement with the molecular formula $C_7H_7NO_2F_6$.

The ir spectrum (KBr) shows a strong band at 3290 $cm^{-1}$ and 1705 $cm^{-1}$ (C=NH). The $^1$H-nmr spectrum (DMSO-$d_6$, 60 MHz) shows the -OH and =NH groups at 8.7 and 7.3 ppm respectively. Two other peaks at 2.6 (2H) and 1.5 (3H) are due to the $CH_2$ group of the heterocyclic ring and the methyl group at position 5.[14] The values of the chemical shifts in the $^{13}$C-nmr spectrum (DMSO-$d_6$) are also in agreement with theoretical values. The imino group carbon appears at 169.3 and 162.3 ppm. The trifluoromethyl groups appear as a quartet at 145.0, 131.0, 116.5 and 102.0 ppm ($J_{CF}$= 300 Hz). The ring carbon atoms attached to the trifluoromethyl groups appear as two quartets at 79 and 75 ppm.

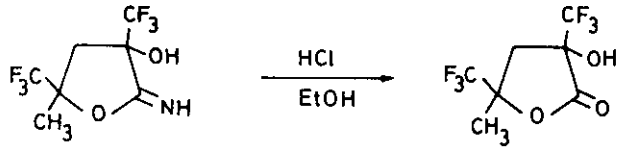
Finally, the methylene and methyl groups appear at 37 ppm and 20.3 ppm respectively.

Scheme 2 summarizes a likely mechanism for the formation of 1. It involves the aldol condensation between two molecules of trifluoroacetone followed by the nucleophilic attack of the cyanide anion to the carbonyl group. Finally, the cyclization takes place through nucleophilic attack by the alkoxide anion to the cyano group, thus leading to the iminooxolane ring.



Scheme 2

The imino group of compound 1 could be hydrolized to carbonyl group, with hydroalcoholic hydrogen chloride, to give 3-hydroxy-5-methyl-2-oxo-3,5-bis(trifluoromethyl)oxolane (2) as an oil in 70% yield.[15] It solidifies with some difficulty to give a solid of mp 57-58°C (Scheme 3).




1 2

Scheme 3

The lactone group of 2 is clearly visible in the ir spectrum at 1800 $cm^{-1}$. The $^1$H-nmr spectrum shows the ring methylene group at 2.70 ppm and the methyl group at 1.65 ppm,[16] together with a peak at 3.62 ppm, which dissappears on addition of TFA, due to the hydroxyl group. Microanalytical (C, 33.37; H, 2.52) and mass spectral ($M^+$ 252) data are also in agreement with structure 2.

ACKNOWLEDGEMENT

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11. To be totally honest, we must tell the whole story: We were trying to extend a synthesis of aminooxolanes from benzylidenemalononitrile and acetone (see reference 12) to trifluoroacetone. We found that benzylidenemalononitrile was not used up in the reaction and did not take part in it. We then decided to investigate this process, with the results described in this paper.
12. J.A. Ciller, N. Martín, M. Quinteiro, C. Seoane, and J.L. Soto, J. Chem. Research (S), 1987, 166.
13. If an additional amount of trifluoroacetone is added to the filtrate, a second crop of product can be obtained.
14. Both the $^{1}$H-nmr spectrum and the $^{13}$C-nmr spectrum show a multiplicity of signals due to the presence of two chiral carbon atoms in the ring, leading to a mixture of diastereomers.
15. The reaction mixture is heated for 30 minutes. Ammonium chloride precipitated on cooling is filtered off, and water added to the filtrate. Compound 2 is collected by extracting with ether.
16. The presence of a diasteromeric mixture is also responsible in this compound for a multiplicity of signals.

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