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PREPARATION AND OXIDATION OF α -NITRO ALCOHOLS WITH SUPPORTED REAGENTS.

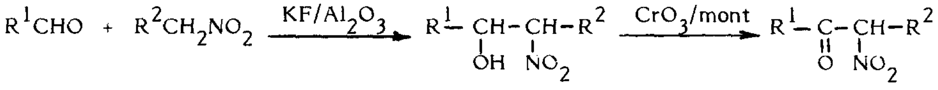
Jean-Marie Mélot, Françoise Texier-Boullet and André Foucaud.

Groupe de Physicochimie Structurale associé au C.N.R.S., Université
de Rennes, Campus de Beaulieu, 35042 Rennes. France.

Summary *- Preparation of 2-nitro alkanols has been achieved by condensation of aldehydes with nitroalkanes in the presence of alumina-supported potassium fluoride. Nitroketones are produced by oxidation of nitroalkanols with montmorillonite - supported chromium trioxide.*

Open chain α-nitroketones are useful intermediates in organic synthesis. However, difficulties are encountered in their preparation and optimization of product yields requires care. Supported reagents can be selective catalysts and enable the course of the reactions to be more easily controlled. We report the synthesis of α-nitroketones from aldehydes and nitroalkanes by using supported reagents.

Base catalyzed nitroaldol condensation (Henry reaction) has been reported, the catalysts being aqueous sodium hydroxide,[1] triethylamine, powdered potassium hydroxide or potassium fluoride and crown ether.[2] This reaction has recently been improved by the use of alumina as catalyst, but remained slow.[3] Alumina-supported potassium fluoride, a catalyst of aldol and Michael reactions,[4] can be used very efficiently to perform the nitroaldol addition yielding 2-nitroalkanols. The reaction times are shorter than with alumina alone, for the same yields.[3] This procedure can be extended to the reaction with aromatic aldehydes, without dehydration of the 2-nitroalcohols into nitroalkenes (nitrostyrenes are generaly obtained when the nitroaldol condensation is conducted in homogeneous medium[11] or with Al_2O_3 [13] which requires long reaction time (table I). The aromatic nitroalcohols are unstable and cannot be purified. They slowly decompose at room temperature to give the nitroalkenes.

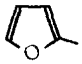


$$R^1CHO + R^2CH_2NO_2 \xrightarrow{KF/Al_2O_3} R^1-\underset{OH}{CH}-\underset{NO_2}{CH}-R^2 \xrightarrow{CrO_3/mont} R^1-\underset{O}{\overset{}{C}}-\underset{NO_2}{CH}-R^2$$

1 **2** **3** **4**

The amount of potassium fluoride on alumina and the catalyst/substrates ratio have a marked influence on the yield of **3**.

Table I - Nitroalkanols **3**

R^1	R^2	Reaction time (h)	**3** % yield [b]
Et	H	5	71
Et	Me	5	75
Me	Et	5	77
i-Pr	Me	5	75
i-Pr	Et	5	78
C_4H_9	Me	5	62
$CH=CMe_2$ $(CH_2)_2CHCH_2$- Me	Me	5	79
	H	5	50
Ph	C_2H_5	6	55
	Me	15[a]	77

[a] Under nitrogen, in the dark. [b] The yields are not optimized.

Alumina-supported (KF, $2H_2O$) (7 g, containing 0.26 g of KF (4.5 mmol) was added slowly, at 0°C, to a mixture of aldehyde **1** (25 mmol) and nitroalkane **2** (25 mmol). The mixture was allowed to stand at room temperature for the reaction time. When the catalyst/substrates ratio was higher or lower, the yield of **3** was lowered.

The oxidation of nitro alkanols into nitroketones has been performed by pyridinium chloroformate,[6] but the reaction is slow. To avoid the retroaldol process and the formation of nitroalkenes, which take place in strongly acidic media, potassium dichromate under phase transfer catalysis has been used.[7] An alternative procedure, more easily to perform, consists in the use of supported CrO_3 (supported permanganate can promote the Nef transformation[12]).

Silica-supported CrO_3 is a catalyst of low stability.[8] Alumina-supported CrO_3 gives poor yields of ketones. The oxidation of **3** can be accomplished with montmorillonite-supported CrO_3.

To a solution of CrO_3 (10 g) in water (50 ml) was added under stirring 20 g of montmorillonite K10. The mixture was dried under reduced pressure (5 torr, 80°C, 24 h). This dry catalyst is stable for two weeks in the dark.

The addition of a small amount of CrO_3/K10 to nitroalkanol is exothermic and can provoke a spontaneous inflammation. Consequently, a solution of nitroalkanol (5 mmol) in CH_2Cl_2 (2 ml) was added at -15°C to a suspension of CrO_3/K10 in CH_2Cl_2 (10 ml). When the reaction mixture was subjected to irradiation with ultrasound,[10] the yield of the isolated nitroketone was markedly improved. The purification of the nitroketone **4** could be achieved by the formation of the dicyclohexylamine salt **5** in 86-95 % yield [9] (table II).

Table II - Oxidation of nitroalkanols **3** into **4**

R^1	R^2	Reaction time (h)	Mass of CrO_3/K10(g)[a]	**4** % yield	**5** m.p.(°C)
Me	Me	3.5	3.5	90[b]	138-140
Et	H	3	3	76[b]	146-147
i-Pr	Me	3	4.3	93[c]	122-123
i-Pr	Et	3.5	3.8	90[b]	99-100

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[a] for 5 mmol of nitroalkanol. [b] The products **4a**[15], **4b**[14] and **4d** are identified by NMR. [c] Mass spectrum, exact mass calcd for $C_6H_{10}NO_3$ 145.0739 found: 145.0761.

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