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FUNCTIONALISATION OF THE α POSITION OF ACRYLATE SYSTEMS BY THE ADDITION OF CARBONYL COMPOUNDS: HIGHLY PRESSURE-DEPENDENT REACTIONS.

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Abstract: aldehydes and ketones will add to acrylonitrile,acrylate esters ,acrolein and α, β -enones with the formation of a range of 2(X)-propen-1-ols (X= CN, COOR, COR). The reactions are catalysed by tertiary amines and are very sensitive to pressure. A wide variety of products may be obtained at pressures of 5 kbar or less whereas most of the reactions do not occur at atmospheric pressure.

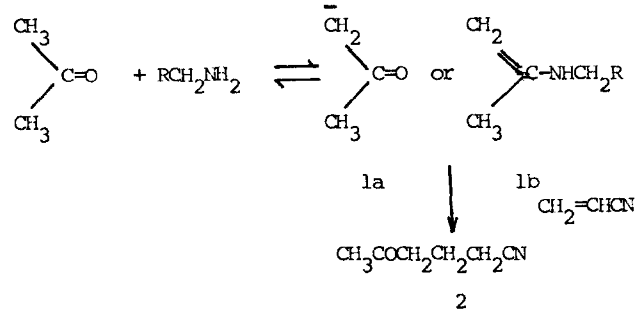
The Michael Addition of acetone to acrylonitrile, Scheme 1, is of industrial importance in the synthesis of pyridine derivatives and is normally catalysed by primary amines. We found the reaction to be strongly accelerated by pressure [1] and, while investigating this aspect of the addition, we also varied the catalyst. It was observed that tertiary amines caused the reaction to take a totally different course resulting in the formation of 3 in high yield rather than 2. α -Substitution of acrylonitrile by acetaldehyde has been claimed in a patent [2] but the reaction is slow. Similarly limited are some analogous reactions of acrylates[3]. In our hands, equimolar quantities of these reagents in the presence of DABCO, the most effective catalyst, react at 25°in the absence of solvent to give 2-cyanobut-1-en-3-ol, (3 ,R_1 = Me) in good yield after 4-5 days. However, the same result can be achieved by maintaining the reagents at 2-3 kbar for 1 hour. Indeed, the reaction is better controlled using the less reactive catalyst,triethylamine.The most likely route to this product is shown in Scheme 2.Addition of the amine to the carbon-carbon double bond leads to a stabilised carbanion which adds in an aldol-fashion to the carbonyl compound. The product then undergoes E2 elimination of the ammonium nucleofuge by attack of a further molecule of base which regenerates the catalyst. The reaction is similar to the base-catalysed polymerisation of acrylonitrile [3], which also is very pressure-dependent.In the presence of an aldehyde, polymerisation is negligible and no Michael adducts are obtained.The reason for the latter observation probably lies in the fact that the reactive species in the Michael addition is the enamine,1b, rather than the enolate,1a. The former would not be possible from a tertiary amine.We have measured rates of reaction of acrylonitrile with acetaldehyde by monitoring the formation of the product 3,R=Me, by gas-liquid chromatography as a function of time at a series of pressures between 1 and 740 bar. Progress of reaction curves were fitted by computer to obtain relative rates,Table 1:

Table 1

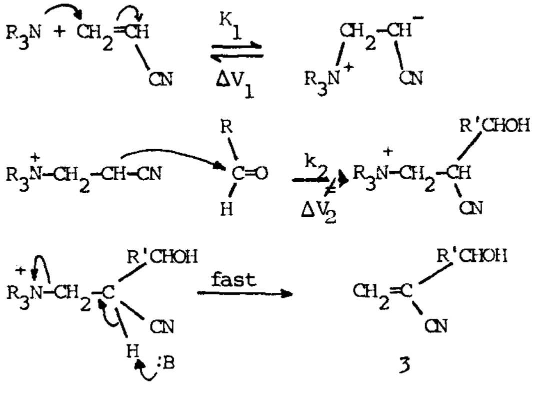
p/bar	1	360	600	740
k_{rel}	1.0	2.9	5.4	8.0

volume of activation = -79 ∓ 5 $cm^3 mol^{-1}$

Scheme 1



Scheme 2



The volume of activation is very large and negative, too great to be associated with a single step process. We assume that the second step of Scheme 2 is rate determining and therefore:

$$\begin{array}{cccc} \Delta V^{\neq}_{obs} = \Delta V_1 & + & \Delta V^{\neq}_2. & \\ -79 \quad (-40 \text{ to } -50) & & (-20 \text{ to } -30) & \text{cm}^3\text{mol}^{-1} \end{array}$$

The volume of reaction for the addition of the amine to acrylonitrile must be very large and negative since a bond is formed and charges separated. That for the addition of the aldehyde also contributes a further reduction in volume on account of the bond-formation. This is one of the most highly pressure-dependent reactions ever observed and this property makes it possible to extend syntheses to analogous reagents which normally are too unreactive to take part. At 1 bar, the only reaction we have been able to observe is that between acrylonitrile and acetaldehyde to yield 2,R=Me and the addition of 2-butenone to acrolein although it has recently been found that certain rhodium catalysts will effect similar

Table 2

High Pressure Additions of Carbonyl Compounds to Acrylic Species

$CH_2{=}CHX + R_1R_2C{=}O \xrightarrow{R_3N} CH_2{=}CH(X)CR_1R_2OH$

	X	R_1	R_2	time/min	p/kbar	yield/%
1	CN	Me	H	5	2-5	90
2	CN	Et	H	5	5	70
3	CN	Ph	H	5	5	95
4	CN	p-An	H	5	5	90
5	CN	H	H	5	2-5	90
6	CN	Me	Me	1000	5	70
7	CN	$-(CH_2)_5-$		1000	5	50
8	COOMe	Me	Me	120	5	75
9	COOMe	Me	Et	120	5	50
10*	CHO	Me	H	25	1.5	95
11*	CHO	Et	H	25	1.5	95
12	CHO	$CH{=}CH_2$	H	30	0.01	20
13	COMe	Me	H	30	5	80
14	$CONH_2$	Me	Me	1000	5	5

(R_3N = DABCO except when indicated *, when Et_3N was used) reactions of enones,[4].

At 5 kbar or less, a wide range of both aldehydes and ketones may be used as the carbonyl component while acrolein,vinyl ketones and acrylate esters may replace acrylonitrile. The products, 2, are highly functionalised and should be useful intermediates for a wide range of syntheses. Qualitatively,the reactivity of the acrylic component falls in the order;

$$X\text{-}CH{=}CH_2\text{:}\quad X= -CHO > -COMe > -CN > -COOR > -CONH_2$$

A β-substituent as is present in crotononitrile, prevents reaction altogether even at 10 kbar. Aldehydes are ,in general, more reactive than ketones and their reactivity falls in the order; MeCHO > PhCHO > n-PrCHO . The catalytic effect of tertiary amines falls in the order; DABCO > quinuclidine > Me_3N > Et_3N, and is probably steric in origin.

Table 2 sets out conditions and yields for representative examples of the α -substitution reaction, which now can be viewed as a synthetic method of wide generality. The modest pressures and short reaction times coupled with excellent yields make this an attractive subject for large-scale synthesis under continuous flow conditions.

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