

# Systematic investigations of the photocatalytic alkyne–nitrile heterotrimerisation to pyridine

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## Abstract

The photocatalytic heterocyclotrimerisation of ethyne and nitrile initiated by cobalt(I) complexes was studied. General mechanistic features as proposed for the 'dark' reaction were found to apply as well under photolytic conditions albeit with modifications. The results suggest that the irradiated light accelerates that stage of reaction, leading to the organometallic species which is believed to be the common intermediate for the formation of pyridine and benzene. The rate of pyridine production is linear dependent from nitrile concentration. Benzene formation may be minimised by keeping the ethyne concentration low. An alternative mechanism, based on the initial coordination of nitrile at cobalt is not confirmed. A novel gas buret system was used, which allowed automatic feed of ethyne under isobaric conditions and to monitor all reactants simultaneously on-line.

**Keywords:** Photochemical activation; Cobalt(I) complexes; Heterocyclotrimerisation; Pyridine-derivatives; Alkynes; Nitriles

## 1. Introduction

Pyridine derivatives, substituted in the 2-position, are of considerable interest in industry and academia [1]. There exist some 'classical' pyridine syntheses [2]; however recent investigations by Wakatsuki and Yamazaki [3,4] and by Bönnemann et al. [5] of the cobalt(I) catalysed cocyclisation of alkynes (two moles) and nitriles (one mole) have led to a new and facile catalytic route providing an improved access to the

pyridine ring system. Whereas both research groups were using more or less unsubstituted alkynes Vollhardt and co-workers [6] developed an advanced and modified strategy allowing the use of substituted alkynes or  $\alpha,\omega$ -diynes and nitriles, or  $\omega$ -alkynyl nitriles and alkynes, respectively, as starting materials and thus made available a variety of more sophisticated ring systems. In most cases  $\text{CpCo}(\text{CO})_2$  was employed as catalyst. First attempts to activate the catalyst by photolysis in the starting phase were undertaken [7].

Generally elevated ethyne pressures and temperatures were used which are prone to create safety risks.

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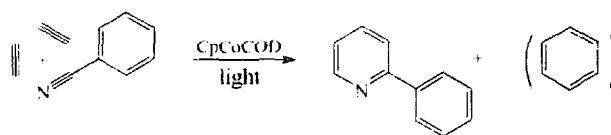
In 1989 our Rostock group observed that these harsh reaction conditions for the ethyne reaction may completely be avoided if the reaction vessel is *continuously* irradiated [8]. Any source of light, even sunlight [8,9], was found to be suitable, the best range of wavelengths being 350–500 nm. Thus the reaction may be conducted under very mild and safe conditions (i.e. *ambient* pressure and temperature) and gives access to a broad spectrum of pyridine derivatives, which, at least potentially, may be interesting for chemical and drug industries. Parts of our synthetic work have been published in preliminary communications [8–11].

Recently, du Plessis et al. [12] reported the cocyclotrimerisation of alkynes and acetonitrile with CpCoCOD as catalyst (thermal and photochemical activation, respectively).

Apart from synthetic concerns mechanistic aspects of the photolytically activated reaction have been of interest to us. We wanted to gain some insight into the photolytically modified mechanism and to find out to which extent it differs from that of the 'dark' reaction.

## 2. Results and discussion

In order to develop basic concepts extensive series of experimental runs were performed un-



der various conditions using CpCoCOD ( $\eta^5$ -cyclopentadienyl- $\eta^1$ -cycloocta-1,5-diene-cobalt(I)) as catalyst precursor and ethyne and benzonitrile as substrates (Scheme 1).

The reactions were studied by determining the time-dependence of the reactants and the brutto-rate-laws; this was done in part by gas-chromatographic determination of the reaction mixtures. Alternatively, the total ethyne consumption was traced under isobaric conditions. For this purpose an advanced new automatic gas buret system, recently developed by us, was used, which, as outlined later, allowed the simultaneous tracking of all reactants, i.e. ethyne, nitrile, benzene and pyridine.

Fig. 1 shows the combined reaction cycles for the cobalt catalysed cocyclisation and homocyclisation reactions as proposed by Bönemann et al. [13,14] for the thermally performed ('dark') reaction on the basis of kinetic and reactivity studies. The key step of this mechanism is a parallel reaction of a five-membered metallacycle with either ethyne or nitrile, lead-

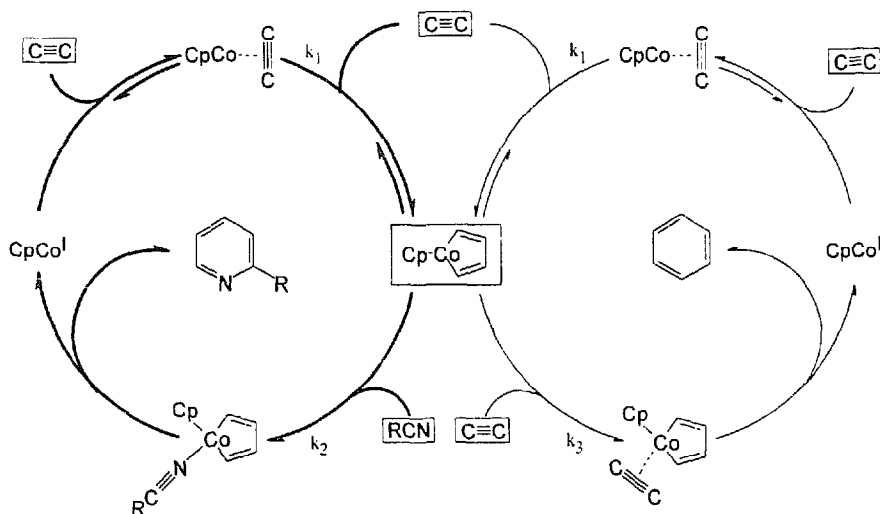


Fig. 1. Reaction scheme for the thermally induced pyridine synthesis according to Bönemann et al. [13,14].

ing to benzene and pyridine, respectively. The reaction is of zero-order kinetic in nitrile and second-order kinetic in alkyne, indicating that the formation of the metallacycle rate-determines the cyclisations [14].

To what extent does this general mechanism apply to the light enhanced reaction? The parallel reactions of the metallacyclic intermediate  $[\text{CpCo}(\text{C}_4\text{H}_4)]^1$  with ethyne and nitrile, respectively, give rise to the following differential equation:

$$\frac{d[\text{N}]}{d[\text{B}]} = -\frac{k_2 \cdot [\text{N}]}{k_3 \cdot [\text{E}]} \quad (1)$$

([N] = nitrile concentration, [B] = benzene concentration, [E] = ethyne concentration,  $k_i$  = rate constants).

If throughout the reaction the ethyne concentration is kept constant and the initial concentration of benzene is zero ( $[\text{B}]_0 = 0$ ) Eq. (1) may be integrated to give

$$\begin{aligned} [\text{B}] &= -\frac{k_3 \cdot [\text{E}]}{k_2} \cdot \ln\left(\frac{[\text{N}]}{[\text{N}]_0}\right) \\ &= -\text{const.} \cdot \ln\left(\frac{[\text{N}]}{[\text{N}]_0}\right). \end{aligned} \quad (2)$$

The nitrile concentrations at  $t = 0$  ( $[\text{N}]_0$ ) were either known or taken from the GC data of the product mixture by

$$[\text{N}]_0 = [\text{N}] + [\text{P}] \quad (3)$$

([P] = pyridine concentration) with  $[\text{P}]_0 = 0$ . This is justified because the selectivity of pyridine formation by nitrile consumption is practically 100% under the experimental standard conditions (see Section 3). Fig. 2 provides an experimental proof of Eq. (3).

The validity of Eq. (2) under photolysis conditions was tested in a lot of experimental runs which were performed under constant pressure, i.e. at *constant ethyne concentration*. Product analysis of samples was done by gas chro-

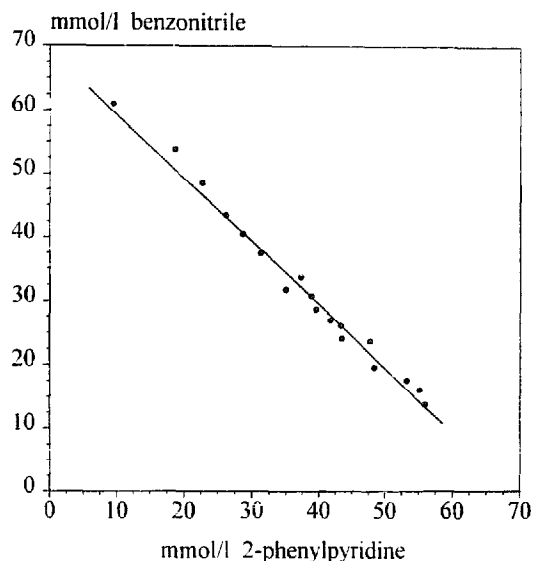


Fig. 2. Plot of benzonitrile- versus 2-phenylpyridine-concentration according to Eq. (3).

matography. The overall result as outcoming is displayed for one example in Fig. 3, showing a linear relationship between [B] and  $\ln([\text{N}]/[\text{N}]_0)$ .

Eq. (2) is valid for different nitrile concentrations  $[\text{N}]_0$  within 0 to 80% of nitrile conversion to pyridine. Linear relationships between  $\ln([\text{N}]/[\text{N}]_0)$  and [B] were indeed always found; variation of the experimental parameters (i.e. reaction temperature, nitrile concentration and intensity of light) did not alter the picture. This however indicates that a parallel reaction exists, by which the products, benzene and pyridine,

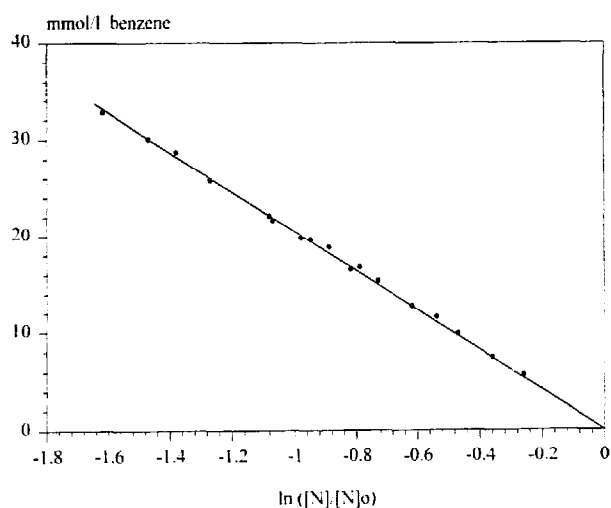


Fig. 3. Plot according to Eq. (2).

<sup>1</sup> For further information on the cobaltacyclopentadiene intermediate see Refs. [3,15–17].

jointly are formed. As a working hypothesis the parallel formation of benzene and pyridine is believed to arise from a metallacyclic species, acting as common intermediate by reacting competitively with ethyne and nitrile. For the obviously investigated parallel-reaction a change of the concentration of the metallacyclic-species as intermediate during the reaction (by e.g. catalyst deactivation) is irrelevant for the product ratio under isobaric conditions. Also the product ratio remains unaltered in the case of polychromatic irradiation instead of the usual monochromatic irradiation for such investigations, if the light only influences the formation of the intermediate.

We were able to monitor the time dependence of the total ethyne consumption under *isobaric* conditions (see Section 3) by means of a computer-linked automatic gas buret system. Tracing the total ethyne consumption during a run showed to be *advantageous* compared with the glc-analytic method since smoother curves drawn from a much larger set of points (minimum time difference between two points only one second) were thus available.

The total ethyne consumption referring to the reaction volume ( $n_E$ ) is described by

$$[n_E] = 3 \cdot [B] + 2 \cdot [P] \quad (4)$$

which, with respect to Eq. (2) transforms to

$$[P] = \frac{1}{2} \left[ [n_E] + 3 \cdot \text{const.} \cdot \ln \left( \frac{[N]_0 - [P]}{[N]_0} \right) \right] \quad (5)$$

By iterative numerical approximation Eq. (5) may be solved for (time dependent) [P]-values when considering the ethyne consumption, the initial nitrile concentration  $[N]_0$  and the slope of the zero-point line according to Eq. (2). We have thus become able to monitor the concentrations of *all* reactants *simultaneously* ([P], by iteration; [N], according to Eq. (3) and [B], according to Eq. (2)). The slope of the zero-point line is determined by one single glc analysis of the mixture at the end of the reaction. The quality of this glc determination is largely decisive for the reliability of the simultaneous tracking of all reactants. However, results obtained from a series of glc-analysed samples compared

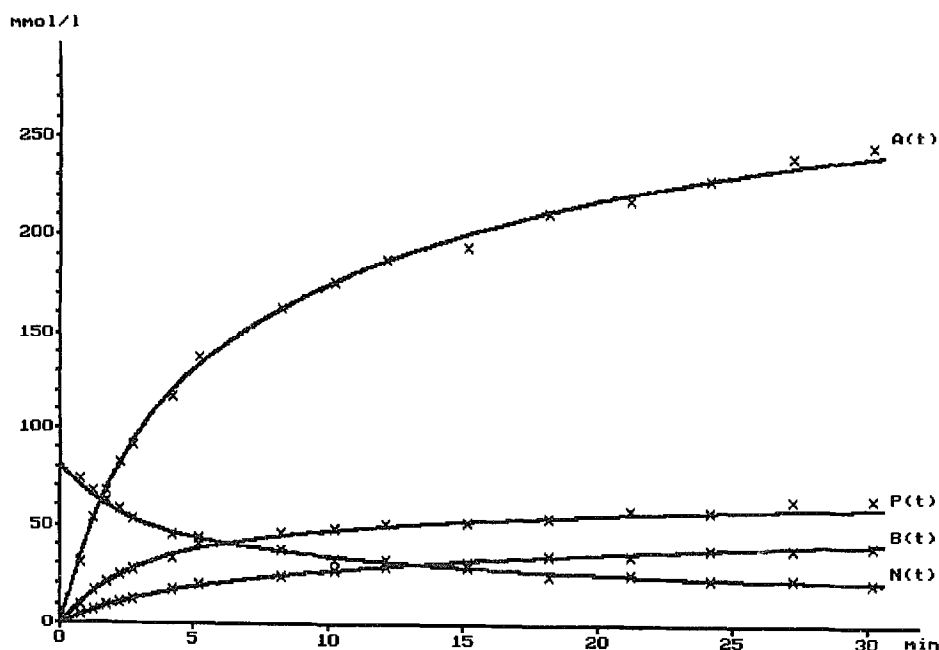


Fig. 4. Graphical curves of benzene (B), nitrile (N), pyridine (P) and alkyne (A), as obtained by GC analysis ( $- \times -$ ) (ethyne according stoichiometry), and from the measured ethyne absorption (filled line) (experimental conditions: 1.21 mmol nitrile, 15 ml of solution).

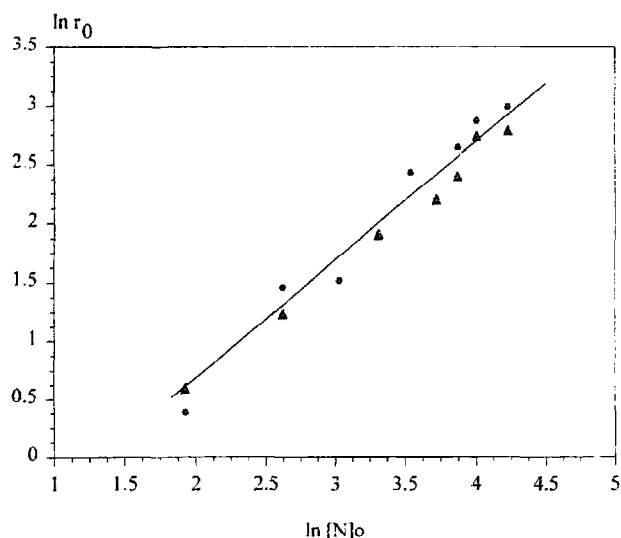


Fig. 5. Nitrile influence from sampling techniques (·) and ethyne consumption (▲) (see Eq. (6)).

nicely with those obtained by the iterative method as shown by Fig. 4.

The initial rate of nitrile decrease ( $r_{[N]_0}$ ) could be determined according to Eq. (6) by considering the initial rates of ethyne absorption ( $r_{[N]_0}$ ) and of the homocyclisation reaction ( $r_{[B]_0}$ ). Unlike in the 'dark' reaction a linear relationship with an slope of ca. 1 between  $\ln(r_{[N]_0})$  and

nitrile concentration  $[N]_0$  was determined (Fig. 5: (▲)). The same result was obtained from the glc-analytic work (Fig. 5: (·)).

$$\begin{aligned} r_{[P]_0} &= \left[ \frac{d[P]}{dt} \right]_{t=0} = \frac{1}{2} (r_{[N]_0} - 3 \cdot r_{[B]_0}) \\ &= - \left[ \frac{d[N]}{dt} \right]_{t=0} = -r_{[N]_0} \end{aligned} \quad (6)$$

Fig. 6 shows some ethyne absorption curves as having been used to clarify the order of the nitrile decrease; a few of them have been omitted for the sake of clarity; the two curves below arise from homocyclisations under the same experimental conditions.

Tracing of the nitrile decrease by monitoring the ethyne absorption showed to be an elegant way to obtain a large number of smooth points from an early stage (~5% conversion of the educt [18]). Accurate initial rates at  $t=0$  have been obtained by fitting the data points to an auxiliary function and evaluating it.

In the 'dark' reaction the formation of the metallacyclic intermediate is believed to be the rate-limiting step, the nitrile reaction order is

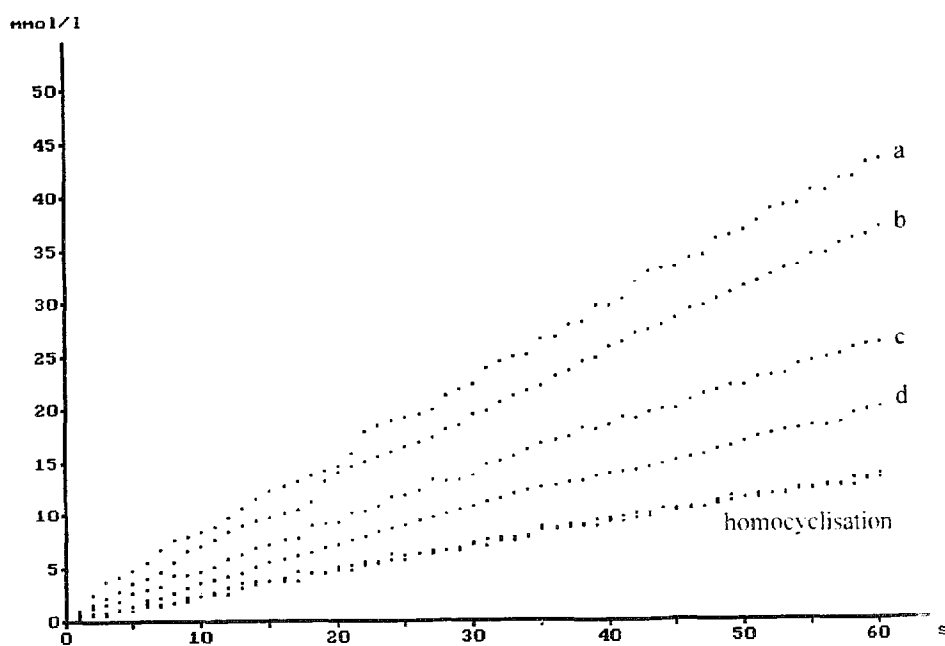


Fig. 6. Ethyne consumption within the first minute of reaction for different concentrations of benzonitrile (a: 68.73 mmol/l; b: 55.00 mmol/l; c: 27.47 mmol/l; d: 13.73 mmol/l).

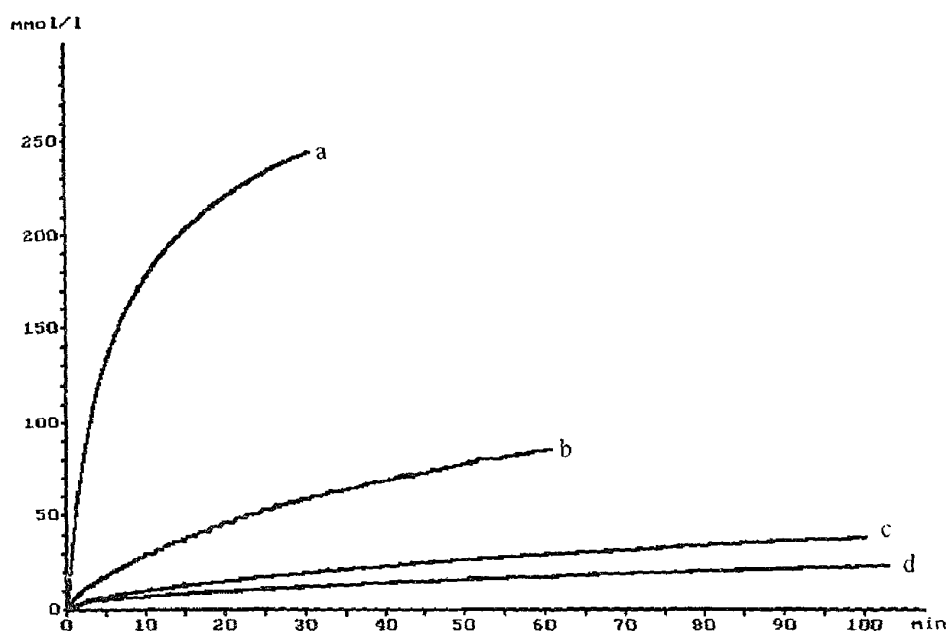


Fig. 7. Ethyne consumption for different COD-additions. a: Without additional COD (standard conditions; see Section 3); b: addition of 0.01 mL COD; c: addition of 0.05 mL COD; d: addition of 0.1 mL COD.

'0'. The linear relationship between the rates of nitrile consumption and the initial nitrile concentrations enlightens one particular aspect of our mechanistic model, namely, that the formation of the metallacyclic intermediate is in the

photochemical reaction *not the rate-limiting step*. The rate-limiting step is rather the reaction of this intermediate with the nitrile, giving thus rise to the observed first-order kinetics. Our 'tentative' conclusion is that the formation of

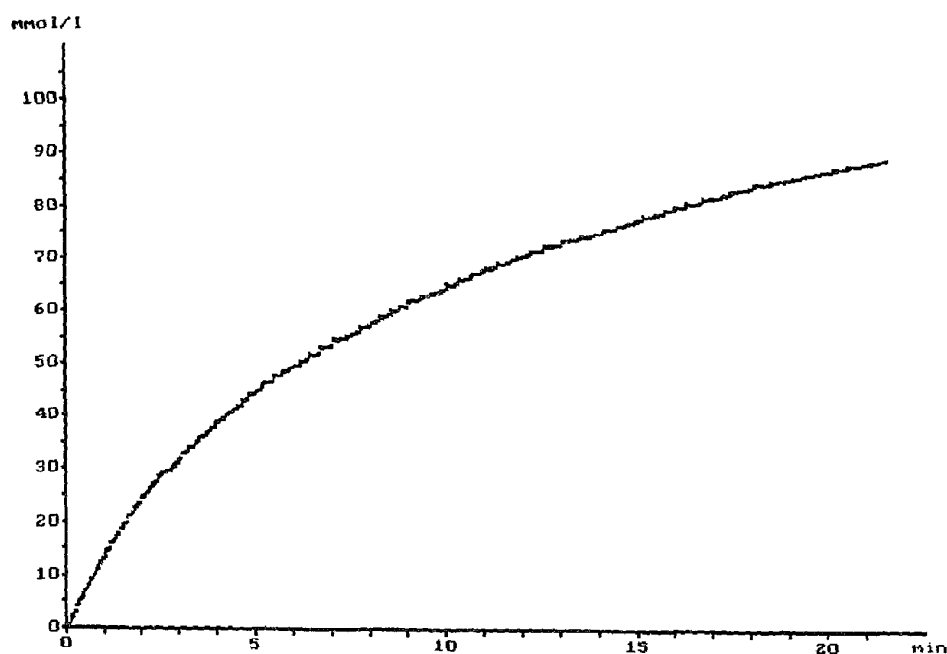


Fig. 8. Ethyne consumption for homocyclisation under standard conditions.

the cobaltacyclopentadiene intermediate, or a step before of it, becomes *accelerated* by the irradiation.

When 'YCoL' (e.g. CpCoCOD) is used as catalyst precursor the thermal pyridine synthesis required a so-called 'start temperature' of about 100°C in order to eliminate the olefin ligand from the coordination sphere of cobalt [5]. In the case of the light enhanced reaction temperatures even below 0°C are sufficient; light obviously causes olefin-elimination from cobalt. On the other hand, addition of free COD causes lowering of the rate of reaction by stabilising the catalyst precursor CpCoCOD and lowering the concentration of reactive intermediates (Fig. 7)<sup>2</sup>.

Decrease of catalyst activity, also well-known for the 'dark' reaction [20], is best noticeable when studying the homocyclisation reaction alone. At constant ethyne and catalyst concentrations the ethyne consumption should be represented by a straight line. Fig. 8 shows the reaction data as obtained under standard conditions; they strongly deviate from linearity even at low conversions which accounts for catalyst deactivation. The latter may likewise be detected from nitrile consumption curves.

Monitoring the homocyclisation reaction provides thus an elegant tool to study the catalyst degradation in more detail under various parameters such as partial pressure of ethyne, solvent, temperature, wavelength of light and to test a variety of catalyst derivatives.

As seen from Eq. (2) the unwanted benzene formation may be kept low by keeping the solution concentration of ethyne at a minimum. This may be done by changing the ethyne partial pressure (the gas buret system allows measurements at low partial pressures) or by using a more suitable solvent. Experiments testing these hypotheses are on the way and results are forthcoming [11].

An alternative pathway for the overall reac-

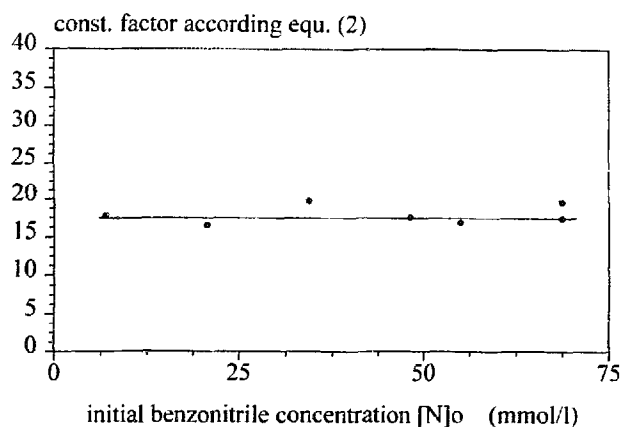


Fig. 9. Slope of the straight line, as experimentally obtained from different initial nitrile concentrations (Eq. (2)).

tion sequence has recently been put forward in the discussion [6,13,21]. Not alkyne (e.g. ethyne) but nitrile is proposed to be the first ligand coordinated at cobalt at the beginning of the cycle. Because such an intermediate cannot, however, yield the homocyclisation product (e.g. benzene) as well, at least two reactive (and competing) intermediates should be present. The ratio between them and therefore the product ratio should be influenced by the alkyne (ethyne) to nitrile ratio. Working with changed nitrile concentrations at constant ethyne pressure (concentration) is quite easy, that is why we did it. Variation of the nitrile to ethyne ratio does not cause the constant factor in Eq. (2) to change, whereas it is likely to do so, if indeed the alternatively proposed mechanism is operational. Whilst we cannot exclude this mechanism to be operational our results do not confirm it. They rather indicate that the constant factor from Eq. (2), upon changing the nitrile to ethyne ratio, remains 'constant', i.e. unaffected, thus rendering the possibility of the alternative mechanism rather unlikely, as far as the photocatalytic reaction is concerned (Fig. 9).

### 3. Experimental

All operations were performed under an atmosphere of prepurified argon. Ethyne was purchased from Linde (99.5%) and passed through

<sup>2</sup> The influence of additional ligands for better precatalyst stability is described recently [19].

$\text{Mn}(\text{NO}_3)_2$  on  $\text{SiO}_2$  [22] in order to remove traces of oxygen and other impurities. Cp-CoCOD was prepared according to literature methods [23]. Benzonitrile, used throughout as substrate, was rigorously dried and distilled under reduced pressure.

**Cyclisations (standard conditions):** A thermostatted reaction vessel, equipped with a teflon-coated spin bar, is connected to a computer-linked automatic and thermostatted gas buret as described basically in [24] and symmetrically surrounded by two 460 W Philips HPM 12 lamps. It is loaded, under exclusion of light, with 13 mL of toluene, 1 mL of a toluene solution containing 1.031 mmol of benzonitrile and 1.031 mmol of *n*-octane (inner standard), and 1 mL of a catalyst/toluene solution containing 0.01031 mmol of CpCoCOD using Hamilton-syringes. The mixture is stirred and saturated with ethyne while protected against light. The lamps are switched on and, after their warm-up (4 min), the vessel is exposed to the

irradiation. Fig. 10 shows a schematical drawing of the experimental set up.

A detailed description of the sampling technic used in several of the cyclisation experiments is given in [24].

Quenching of the reaction was done by switching off the lamps and introducing air simultaneously. The solutions were subsequently analysed by glc using a HP 5890 II with an OV 101 (length 12 m; temperature program: 10 min isotherm at 35°C, heating rate 10°C/min up to 200°C; carrier gas argon; gas stream 1 mL/min).

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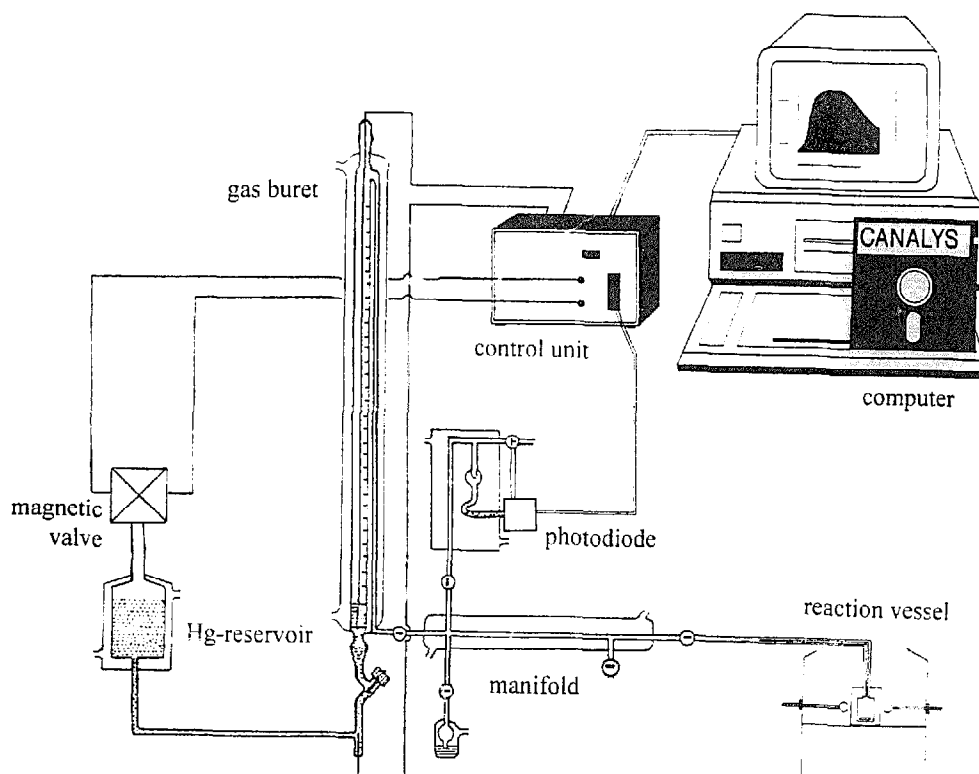


Fig. 10. Schematical drawing of the experimental apparatus.



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