hypothetical monomer 3 with a free NH-proton is estimated to be δ^H_m 3 = δ_m 5, considering the stronger electron accepting properties of the acetyl group in comparison to the methyl group. Thus, the chemical shift δ_{ch} for the hydrogen bonded interaction in 5 is calculated to be 195 Hz, after making corrections for anisotropic effects of the amide group [7] and assuming $\Delta\delta = \delta_{aniso.} + \delta_{ch}$. Since the strength of hydrogen bonding did not differ greatly in the inter- and intramolecular case [5], the hypothetical NH-resonance of the intramolecular bondes monomer 3 is roughly 700 Hz without anisotropic shifts. The observed value δ_m = 647 Hz is possible only as a result of an anisotropic upfield shift, typical of hydrogen bonding with π-acceptors. [8]

Further support for structure 7 in monomer 1-3 was obtained by the influence of alkyl groups on K_D and δ_m. Although the behaviour within the dimerisation is identical in 1 and 2 (K_D 1 $\approx$ K_D 2), the nitrogen proton of intramolecular H-bonded 3 is more strongly shielded than in 2. We propose a steric compression of the NH-proton toward the π-electrons of the α-carbonyl group. This compression increases further in 4, corresponding to a particularly strong intramolecular hydrogen bond [9]. But the increase in the upfield shift by the nearer anisotropic center will be opposed in this case by the lowfield shift due to stronger H-bonding.

The results support an intramolecular hydrogen bonding of structure 7 in N-alkylpyruvamides and probably in other α-oxo acid amides too.

References:

1. G.Fischer, G.Oehme and A.Schellenberger, Tetrahedron 27, 5683 (1971)
2. L.L.Graham and C.Y.Chang, J.Phys.Chem. 75, 776 (1971)
3. U.Jentschure and E.Lippert, Ber.Bunsenges.physik.Chem. 75, 557 (1971)
4. P.Schuster, Z.Chem. 13, 41 (1973)
5. G.Fischer, unpublished
6. W.A.P.Luck, Naturwissenschaften 54, 601 (1967)
7. D.P.Eyman and R.S.Drago, J.Amer.Chem.Soc. 88, 1617 (1966)
8. G.L.Hofacker and U.A.Hofacker, Coll.Ampere XIV, North-Holland Publ.Co., 1967, 503
9. H.Musso and K.-H.Bantel, Chem.Ber. 102, 686 (1969)

Tetrahedron Letters No. 37, pp 3311 - 3314, 1974. Pergamon Press. Printed in Great Britain.

TRANSITION METAL CATALYZED 1-3-DIPOLAR CYCLOADDITION OF CARBETHOXYCARBENE TO ACRYLONITRILE *

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Ketocarbenes are known to undergo spontaneously Wolff rearrangement rather than intermolecular reactions; in the presence of copper catalysts however, they react as a bivalent reagent either as a carbenic species (leading e.g. to cyclopropanation of olefins), or as a 1.3-dipole by adding to various substrates such as olefins (1), acetylenes (2), ketene (3), acetone (4), carbon disulfide, phenyl isothiocyanate (5) or nitriles (6,7). With nitriles, oxazoles are generally formed but yields are rather poor when the ketocarbene is produced either by photolysis or by thermolysis of diazocompounds and are only slightly improved by use of copper catalysts (8).

Moreover, the extension of these results to polyfunctional nitriles failed, up to now, because of the low reactivity of the nitrile group relative to other functions such as olefinic groups : for example, only Δ^2 pyrazoline 2 is obtained (65 % yield) when acrylonitrile is allowed to react with ethyl diazoacetate at room temperature without any catalyst (9). (The correct structure of 2, different from those reported in the literature , has been ascertained by i.r. and n.m.r. spectroscopy (10)). In contrast, we have found that, at temperatures higher than 100° C., cyclopropanation takes place quantitatively. These interesting observations may be interpreted by a prior formation of the Δ^1 pyrazoline 1 which is readily isomerised to its Δ^2 isomer at room temperature, whereas direct decomposition to cyclopropane derivatives occurs at higher temperature (Δ^2 pyrazoline never decomposes to cyclopropanes).

In a recent investigation of the influence of transition metal complexes on the selectivity of typical reactions of carbenes, we have already shown that cyclopropanation of olefins (11), as well as insertion in polar X-H bonds (X = O, S, NH) were very efficiently catalysed by palladium and rhodium complexes (12).

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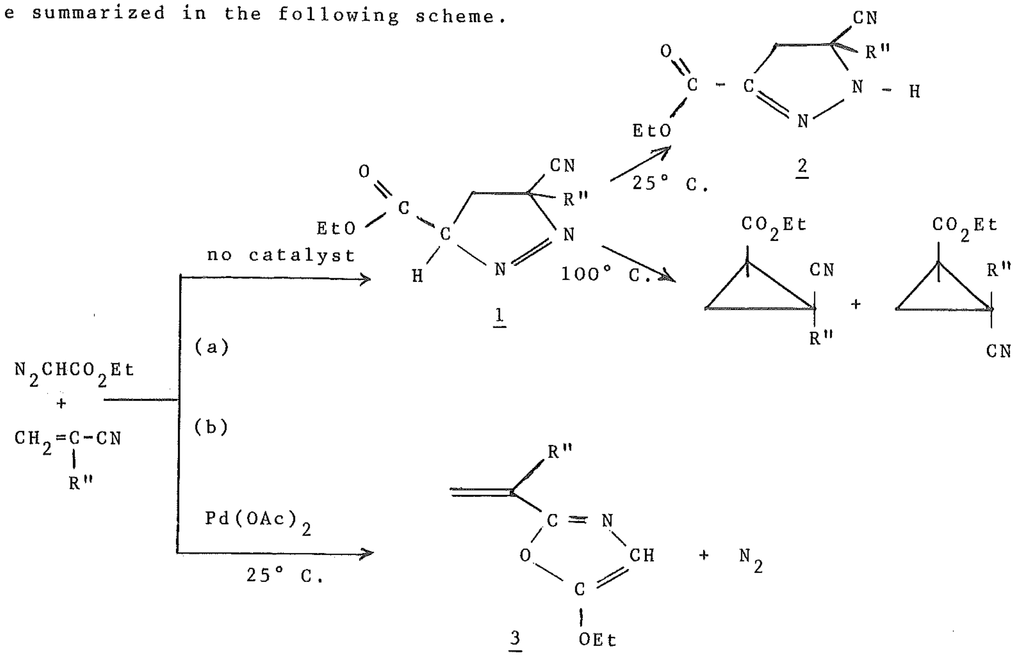
* For the previous papers in the series, see references 11 and 12.

We have consequently examined the influence of these transition metal catalysts on the reaction of diazoacetates and nitriles, and we have put in evidence a definite effect of palladium(II) acetate on reaction (b) (palladium chloride and cyanide are much less efficient catalysts). Acetonitrile, benzonitrile and benzylcyanide react at room temperature to give oxazoles in 22, 28 and 20 % yield respectively. However, the most interesting behaviour, not observed with usual copper catalysts, is obtained with acrylonitrile (R" = H) and methacrylonitrile (R" = CH_3) which form the corresponding 2-vinyl-5-ethoxy-oxazoles 3 (reaction b) with complete exclusion of pyrazoline 2. The results are summarized in the following scheme.



In a typical run for synthetical purpose, ethyl diazoacetate (0,05 m) is added slowly (over 24 hrs) to a well-stirred solution of $Pd(OAc)_2$ (0,001 m) in nitrile (0,5 m). Evaporation of the solvent and distillation afford the oxazole in 30 % yield.

3 (R" = H and CH_3) have been identified by elemental analysis and spectroscopic data. In particular, H^1NMR spectra of 3 (R" = H) in CCl_4 shows a typical ABC styrene-type system with three quartets centered respectively at δ = 5.32, 5.79 and 6.30 ppm in addition to the triplet (δ = 1.35) and the quartet (δ = 4.04) of the ethoxy group and the singlet (δ = 5.93) corresponding to the methine proton of the cycle.

In the same solvent, 3 (R" = CH_3) exhibits an AB system centered at 5.08 and 5.57 ppm in addition to a multiplet at 1.99 (2 H.), a triplet at 1.35 (3 H.), a quartet at 4.02 (2 H.) and a singlet at 5.92 (1 H.)

The polymerization of these two novel oxazoles, which are not accessible by other straightforward methods, is presently studied in our laboratory.

From the reaction mixture, ethyl maleate, ethyl fumarate and polyketocarbenes were also identified.

This last well-characterized polymeric material represents an important part of the initial diazoacetate. The other reactions occur only in the presence of the catalyst, whereas pyrazoline 2 is the sole product formed in its absence. It is characteristic of a competitive coordination reaction that the yields in 2 drop considerably when catalyst concentration increases, whereas the yields in oxazoles increase progressively. Less palladium acetate is needed with methacrylonitrile than with acrylonitrile to get the best yield in oxazole; on the other hand, in the absence of any catalyst, the kinetics of the reaction indicate a much greater rate for the formation of 2 in the case of (R" = H) than when (R" = CH_3). The difference between acrylonitrile and methacrylonitrile may therefore be interpreted as the result of the greater sensitivity to steric hindrance in the pyrazoline reaction than in the catalytic steps leading to the oxazoles (13).

All of these observations fit with a mechanism involving the easy decomposition of the diazocompound through coordination on palladium, with formation of an intermediate coordinated ketocarbene undergoing further rearrangements. Such a coordinated ketocarbene would be responsible for the formation of polyketocarbene, ethyl maleate and fumarate as well as of oxazole in the catalytic process.

It is also significant that the selectivity in oxazole formation is notably improved by a slow addition of diazoacetate to the nitrile (see preparative procedure) : this is a good indication that the ratio diazoester/catalyst must be kept as close as possible to stoichiometry in order to avoid the formation of 2 by the uncatalysed reaction involving the free diazocompound. Moreover, the formation of polymers is also disfavoured as expected.

Some activation of the nitrile group, through coordination with the metal, contributes most probably to the observed selectivity (14).

Preliminary attempts to isolate the complexes led to precipitation of the metal, whereas the formation of by-products prevent any more detailed mechanistic approach of the reaction.

However, these results stress again the usefulness of coordination catalysis in fine organic synthesis.

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References

1. G. Binsch, R. Huisgen and H. König, Chem. Ber., 97, 2893 (1964).
2. R. Huisgen, G. Binsch and H. König, Chem. Ber., 97, 2884 (1964).
3. W. Ried and H. Mengler, Am., 678, 113 (1964).
4. H. Dworschak and F. Weygang, Chem. Ber., 101, 289 (1968).
5. R. Huisgen, G. Binsch and H. König, Chem. Ber., 97, 2868 (1964).
6. R. Huisgen, H.J. Sturm and G. Binsch, Chem. Ber., 97, 2864 (1964).
7. M.I. Komendantov, V.N. Novinsky, R.R. Bekmouchametov, J. Org. Chem. USSR, 9, 427 (1973).
8. W. Kirmse, "Carbene Chemistry" 2nd ed., Acad. Press, New York, N.Y. 1971.
9. S.M. Gurvitch and A.P. Terentev, Sbornik Statei Obshchei Chim., 1, 409 (1953); C.A., 49, 1047^i (1955).
10. R. Paulissen, to be published elsewhere.
11. R. Paulissen, A.J. Hubert and Ph. Teyssié, Tetrahedron Letters, 1465 (1972).
12. a) R. Paulissen, H. Reimlinger, E. Hayez, A.J. Hubert and Ph. Teyssié, Tetrahedron Letters, 2233 (1973).
    b) R. Paulissen, E. Hayez, A.J. Hubert and Ph. Teyssié, Tetrahedron Letters, 607 (1974).
13. R. Huisgen, H. Stangl, H.J. Sturm and H. Wagenhofer, Ang. Chem., 73, 170 (1961).
14. G.N. Schrauzer, J. Amer. Chem. Soc., 81, 5310 (1959).

Tetrahedron Letters No. 37, pp 3315 - 3318, 1974. Pergamon Press. Printed in Great Britain.

BIOSYNTHESIS OF COLCHICINE: INCORPORATION OF A ^{13}C-LABELLED PRECURSOR IN A HIGHER PLANT

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Researches based on carbon-13 labelling combined with ^{13}C-n.m.r. have already proved powerful for the study of biosynthetic pathways.[1] Not only is the labelling pattern directly revealed by the n.m.r. spectrum (provided unambiguous assignments of the signals can be made) but with appropriate design of the experiment, the spectrum can yield additional information of crucial importance.[2] However, the technique has only been used so far with partially purified enzyme systems[2] or with micro-organisms.[3] The difficulty in applying ^{13}C-labelling to studies of higher plants arises from the low