

Photochemistry of pyridyl azides and diazo ketones in matrix and in solution

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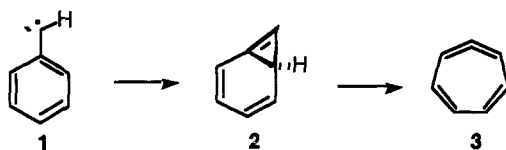
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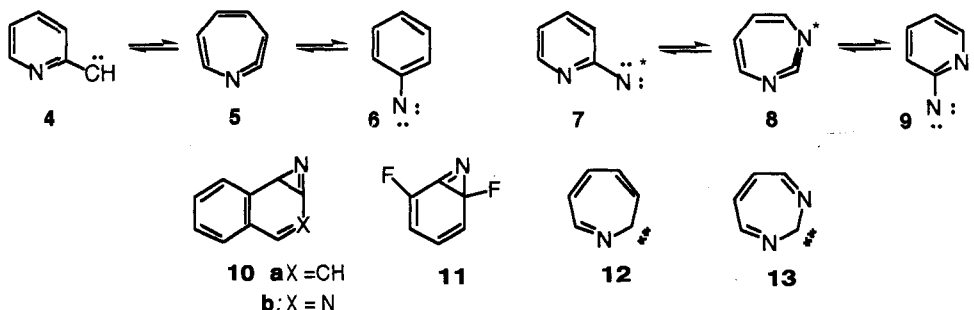
Abstract: This paper describes recent advances in the photochemistry of 2-pyridyl azides/tetrazolo[1,5-*a*]pyridines, which is a viable synthetic source of novel 1,3-diazepines via ring expansion of the 2-pyridylnitrenes to 1,3-diazacycloheptatetraenes. The nitrenes have been observed by Ar matrix ESR spectroscopy, and the diazacycloheptatetraenes by Ar matrix IR spectroscopy. Trapping with nucleophiles in solution at room temperature leads to 1*H*-1,3-diazepines, some of which are stable, distillable compounds, whereas others isomerize to stable 5*H*-1,3-diazepines. New chemistry in the field of Wolff rearrangement of pyridine-based diazoketones leads to 2- and 3-azafulvenones, which dimerize or tetramerize at extremely low temperatures (40 - 70 K). These facile reactions are thought to involve ketene-nucleophile ylide (zwitterion) intermediates. It was found that ketenes react with pyridine to form related ylides at temperatures as low as 15 - 40 K.

INTRODUCTION

The rearrangements and interconversions of arylcarbenes and arylnitrenes have been the subject of several reviews (1), and the energy surface connecting the phenylcarbene isomers (1 - 3 and others) has recently been studied in considerable detail by theoretical calculations (2).

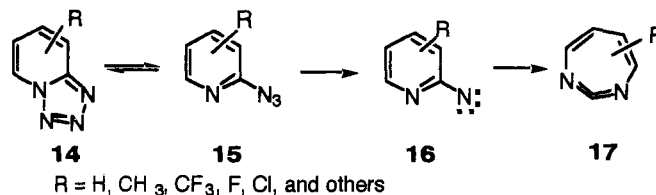


The interconversions of 2-pyridylcarbene (4) with phenylnitrene (6) and the automerization of 2-pyridylnitrene (7) were the first rearrangements of this kind to be recognized (3), and it is now well established that they take place via seven-membered allene-type intermediates, 5 and 8, respectively (1,2,4). The reactions can be carried out both photochemically and thermally, from azide or diazo compound precursors, and the intermediates 5 and 8 have been isolated in low temperature matrices and observed by IR spectroscopy under both sets of conditions (1,4-6). The question of involvement of bicyclic intermediates of the type 2 has been discussed in the literature (1,6), but they have only been observed directly in benz-annulated (1*f*,7) (10) and *ortho*-fluorinated (11 and the pentafluoro analog) (8) cases and will, for the sake of brevity, not be invoked further in this article. For questions of the possible existence and role played by (singlet and/or triplet) carbene intermediates of the types 12 and 13, the reader is referred to the original literature (2,6,9).

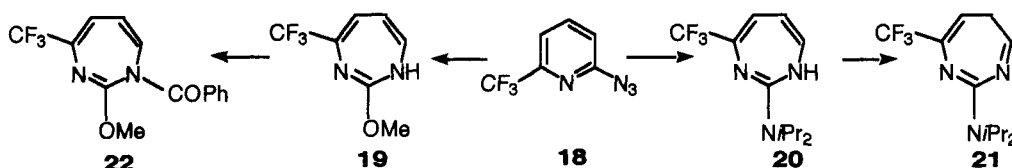


1,3-DIAZEPINE FORMATION

Tetrazolo[1,5-*a*]pyridines (**14**) exist in valence-tautomeric equilibria with 2-azidopyridines (**15**). In the unsubstituted case, this equilibrium lies far on the side of the tetrazole, so that the azide cannot be detected at all at ordinary temperatures; however, simple sublimation of the tetrazole causes conversion into the azide, which can be condensed at liquid nitrogen (or lower) temperature (5). Electron-withdrawing substituents appear to favor the azide forms, and the 6-trifluoromethyl derivative **18** exists exclusively as an azide at room temperature (6). For the subsequent generation of the seven-membered ring carbodiimides **17**, it is immaterial whether the tetrazole or azide form has been produced, as Ar matrix photolysis (broadband; usually employing a 1000 W high pressure Hg/Xe lamp) of both rapidly generates the nitrenes **16** (observed in their triplet states by Ar matrix ESR spectroscopy at ca 12 K) and the carbodiimides **17**. The latter are formed virtually quantitatively according to Ar matrix IR spectroscopy where they absorb strongly in the region of 2000 cm^{-1} . In the case of 3,5-bis(trifluoromethyl)-2-pyridyl nitrene, the nitrene was also observed by IR spectroscopy, but it, too, was converted to the cyclic carbodiimide on further photolysis (6).

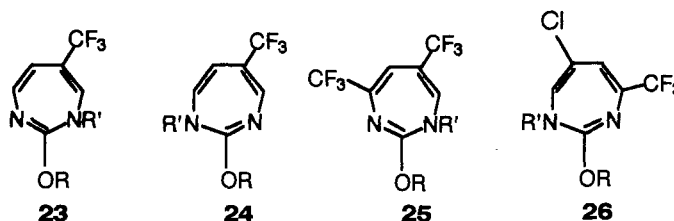


Much of our work on the trapping of these cyclic carbodiimides to produce 1,3-diazepines has used trifluoromethyl-substituted substrates and such examples will be given below, but this is by no means a limitation. The parent substance as well as methyl-substituted derivatives undergo the same reactions.



Thus, photolysis of azide **18** for 80 min in dioxane-methanol solution at room temperature gave a 92% isolated yield of the distillable 1*H*-1,3-diazepine **19** (10). Similar trapping with secondary amines proceeded analogously, e.g. giving the diisopropylamino derivative **20** in 76% yield. However, this compound isomerized to the 5*H* analog **21** at 100 °C (10). Results so far suggest that the 1*H* forms of alkoxy-substituted 1,3-diazepines are configurationally more stable than the amino analogs, but it is emphasized that the 1*H* tautomers can be isolated in both cases. Proof of the 1*H* structure follows not only from ^1H and ^{13}C NMR spectroscopy, but also from the X-ray crystal structures of the 1-benzoyl derivative of **19** (**22**) (10) as well as a 1-unsubstituted 1*H*-1,3-diazepine (11).

Numerous 1,3-diazepines containing mono- and bis-trifluoromethyl, chloro, alkoxy, and dialkylamino substituents have been prepared in this manner (10,11). Some further examples are shown below (**23-26**).

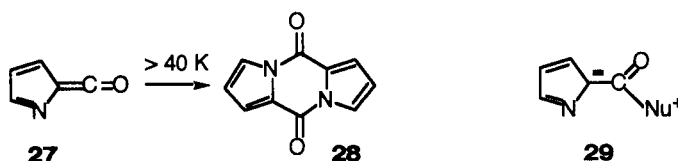


Extension to the synthesis of benzo-1,3-diazepines from azido/tetrazoloquinolines and -isoquinolines, and of benzotriazepines from azido/tetrazoloquinazolines and -quinoxalines is in progress (11). The matrix photochemistry and IR observation of the seven-membered ring carbodiimide intermediates have been performed (11).

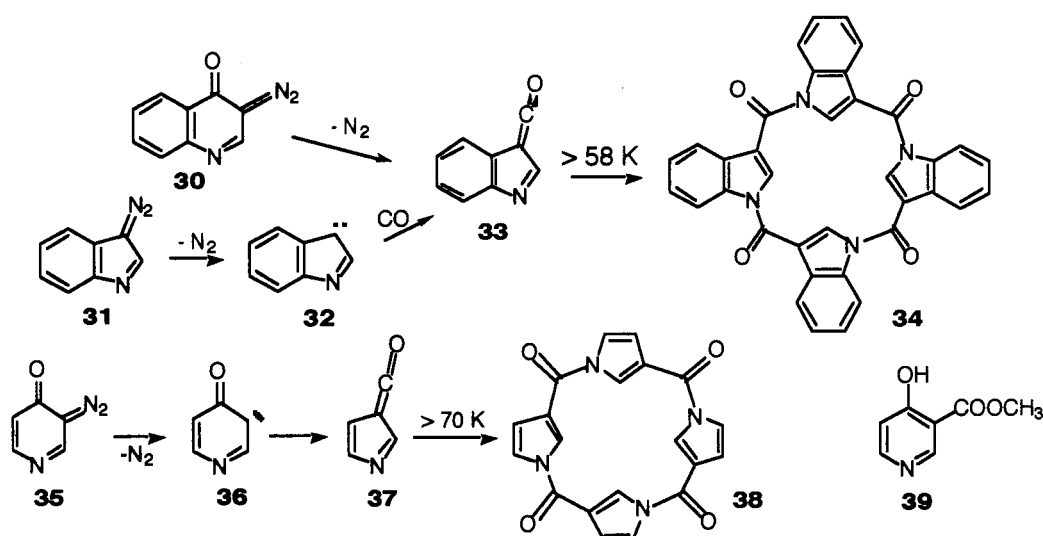
The mechanism of addition of nucleophiles to the cyclic carbodiimides is presumably analogous to the interaction between ketenes and nucleophiles, which will now be examined in some detail

AZAFULVENONES AND KETENE TETRAMERIZATION

The second topic of this lecture is concerned with the photochemical Wolff rearrangement of pyridine-based diazo ketones. We have reported (12) that (thermally generated) α -azafulvenones dimerise at extraordinarily low temperatures, namely 40–70 K (e.g. **27** \rightarrow **28**), and we theorized that this was due to one molecule of the ketene acting as an *N*-nucleophile toward another, thus generating a so-called ketene–nucleophile ylide (correctly zwitterion) (**29**), which rapidly ring closes to form the dimers.



The question then arose what would happen if the ring nitrogen was in the β -position in the azafulvenone. It turned out that the ketene (**33**) now tetramerized to give the “tetra-*N*-confused” (13) porphyrin analog **34** very efficiently and again at very low temperature (ca 58 K) as determined by IR spectroscopy (14). The required ketene **33** was generated by matrix photolysis of diazo ketone **30** but is also formed on flash vacuum thermolysis of the same compound. Another route of photochemical but no preparative interest is the trapping of carbene **32**, formed by irradiation of diazo compound **31** in CO matrix (14,15).

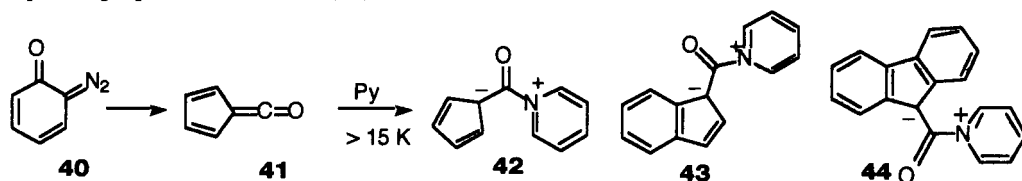


A similar methodology was used to prepare the parent ketene **37** and its tetramer **38**. The diazo pyridone **35** underwent photochemical Wolff rearrangement to **37** in nitrogen matrix at 12 K (the carbene **36** was not observed). **37** tetramerized to **38** on warming to 70 K. In order to obtain **38** in preparatively useful quantities, a different method based on flash vacuum thermolysis of the simple 4-hydroxynicotinate **39** was developed (14).

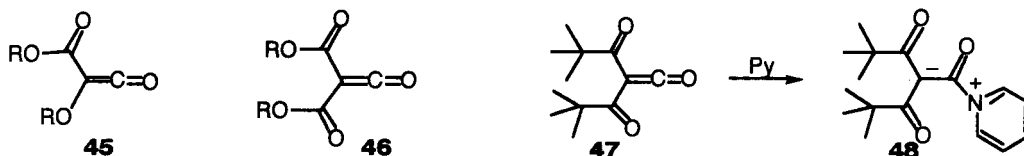
KETENE–PYRIDINE YLIDES

In the reactions between cyclic carbodiimides and nucleophiles described in the first section of this paper, an “ylide” (zwitterion) analogous to **29** can be postulated. We believe the extraordinarily facile dimerizations and tetramerizations of nitrogen-containing ketenes such as **27**, **33**, and **37** are due to similar transient ketene–nucleophile ylide formation. We therefore set out to synthesize and observe the related ketene–pyridine ylide **42** as well as the corresponding benzo and dibenzo derivatives **43** and **44** using photolytic Wolff rearrangements of the requisite diazo ketones (**40** and benzo derivatives) in pyridine matrices at temperatures below 12 K. The ketenes can indeed be generated and observed by IR spectroscopy under these conditions, even though they react extremely readily with pyridine, in the case of the monocyclic ketene **41** already at a temperature of 15 K. The reactions were monitored by IR spectroscopy; the ketenes

(and pyridine) disappeared at the same rates as the ylides were formed, the latter absorbing in the region of 1653–1683 cm^{-1} in the IR (16). The IR spectra of the ylides are in good agreement with DFT calculations incorporating a polar solvent field (17).



Furthermore, this work has been extended to photochemically and/or thermally generated α -oxo ketenes **45** - **47**, which form ylides (e.g **48**) with pyridine at temperatures of 40 - 100 K (17).



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