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The mechanism of the prototype cation radical cycloaddition reaction: the cyclodimerization of *N*-vinylcarbazole

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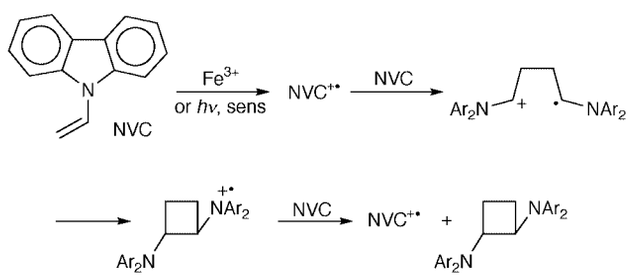
The mechanism of the first cation radical cycloaddition reaction to be discovered, the cyclodimerization of *N*-vinylcarbazole, has now been studied by means of a stereochemical criterion. The cyclodimerization of *N*-(*cis*-2-deuteriovinyl)carbazole is observed to be non-stereospecific, yielding a cyclodimer in which approximately 80% of the deuterium atoms are *cis* to the carbazolyl group and 20% are *trans* to the carbazolyl group. This result stands in contrast to the stereospecific cyclodimerization of *trans*- and *cis*-anethole and other stereospecific cation radical cyclobutanation reactions which have been studied more recently. The cyclodimerization of *N*-vinylcarbazole must therefore occur *via* a stepwise path, involving an intermediate distonic cation radical, as originally proposed by the Ledwith group. Further, the *gauche* conformation of the distonic cation radical is implied to be preferred over the *anti* form.

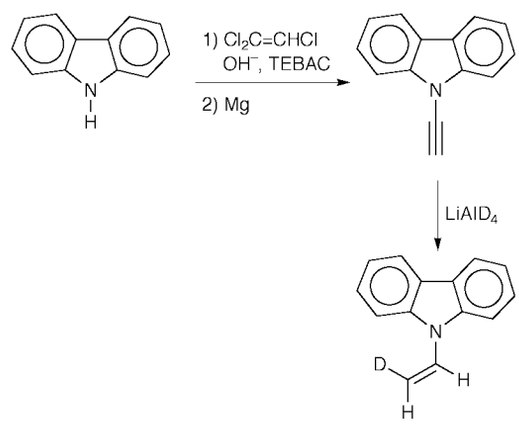
The cyclodimerization of *N*-vinylcarbazole in methanol solution in the presence of ferric ion is the prototype, classic example of a cation radical chain cycloaddition reaction (Scheme 1).[1] The mechanism envisioned by the Ledwith group



Scheme 1 The cation radical chain cyclodimerization of *N*-vinylcarbazole.

for this cycloaddition was a stepwise one involving an intermediate in which the cationic and radical sites are essentially separate (a distonic cation radical). The analogous cyclodimerization of *N*-(*trans*-propenyl)carbazole was also observed to proceed, but the corresponding reaction of *N*-(*cis*-propenyl)carbazole failed. The stepwise mechanism was therefore proposed without the benefit of a stereochemical probe and, apparently, without other direct experimental support. Subsequently, the cation radical cyclodimerization of *cis*- and *trans*-anethole, which is an analogous cyclobutanation reaction, was found to be stereospecific and therefore consistent with a concerted cycloaddition mechanism.[2,3] More recently, still further examples of stereospecific cation radical cyclobutanations have been observed.[4] It therefore appeared especially important to determine the stereochemistry of the prototype cation radical cycloaddition to provide insight into the mechanism of this important reaction, and more specifically to investigate whether the stereochemical criterion would support the proposed stepwise nature of this historic cyclodimerization.

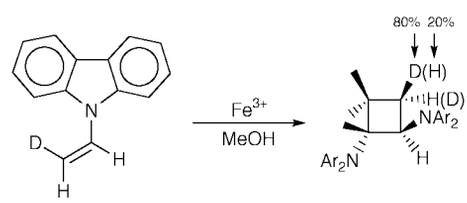
The object of the present research was thus to prepare and cyclodimerize an *N*-vinylcarbazole substrate which is stereospecifically (*cis* or *trans*) labelled by deuterium at the 2-position of the vinyl group. For this approach to succeed it was of course necessary that the methylene protons which are respectively *cis* and *trans* to the carbazolyl moiety on the cyclobutane ring of the dimer have different chemical shifts and be well resolved from each other in the proton NMR. This requirement was well satisfied, the *cis* protons absorbing at δ 3.08 and the *trans* protons at δ 2.74. The *N*-(*cis*-2-deuteriovinyl)carbazole monomer was then synthesized from carbazole *via* a three step sequence (Scheme 2).[5] The key step of this sequence was



Scheme 2 Synthesis of *N*-(*cis*-2-deuteriovinyl)carbazole.

the (*trans*) stereospecific reduction of *N*-ethynylcarbazole with lithium aluminum deuteride.[6]

The cyclodimerization of the stereospecifically deuterated *N*-vinylcarbazole was then carried out under the conditions previously used by the Ledwith group (Scheme 3). Since the



Scheme 3 Cyclodimerization of labelled *N*-vinylcarbazole.

reaction is quite fast, it was necessary to quench the reaction mixture at relatively short reaction times using sodium thiosulfate solution, in order to observe the stereochemical composition of the dimer under conditions in which the stereochemical composition of the unreacted monomer could also be determined. When the reaction was carried out for reaction times of 30, 60, and 70 s, careful integration of the *cis* and *trans* methylene proton peaks of the dimer revealed, respectively, that 82, 80.6, and 80% of the methylene protons were of the *trans* variety (retention of stereochemistry), while 18, 19.4, and 20% of the methylene protons were of the *cis* variety (inversion of stereochemistry). Under all of these conditions it was determined that the recovered labelled *N*-vinylcarbazole had not undergone stereoisomerization to the *trans* isomer.

The same cyclodimerization was also carried out under photosensitized electron transfer (PET) conditions, using acetonitrile as the solvent and dicyanobenzene as the sensitizer. Once again, the reaction is impressively fast, achieving conversions of 70–80% after only 5 minutes of irradiation and being essentially complete within 20 minutes. When the labelled substrate was subjected to irradiation for just three minutes, 81% of the methylene protons of the dimer were found to be *trans* to the carbazolyl group and 19% were *cis*. Under these conditions, the recovered *N*-vinylcarbazole was confirmed to be the pure (un-isomerized) *cis*-deuterio substrate. These observations are in excellent agreement with those found for the ferric ion catalyzed reaction.

The present results provide decisive support for the assumption of a distonic cation radical intermediate in the cycloaddition of the *N*-vinylcarbazole cation radical to neutral *N*-vinylcarbazole. Further, since the stereorandomization in the distonic cation radical is far from complete, it is apparent that cyclization of the latter is competitive with and even somewhat faster than stereorandomizing bond rotations. This rapid cyclization appears much more plausible for a *gauche* (cisoid) cation radical than for an *anti* (transoid) cation radical. Although the non-stereospecificity of the cyclodimerization reaction implies the absence of a significant covalent interaction between the carbocation and radical sites in the distonic intermediate, the apparent preference for a cisoid intermediate over a transoid one suggests the possibility that there is a significant electrostatic attraction between the two termini in the cisoid form.

A final note of interest is the contrast between the stereochemical results in the dimerization of *N*-vinylcarbazole and those for other cyclobutanations, including the anetholes. We regard this contrast as not at all unexpected because of the exceptionally strong stabilization of the carbocation moiety by a strongly electron donating amino function, which effect might be expected to preferentially stabilize the distonic intermediate having a localized positive charge.

Acknowledgements

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