Diels–Alder cycloadditions of the *N*-vinylcarbazole radical cation

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The first radical cation Diels–Alder reactions of *N*-vinylcarbazole, the substrate for which radical cation cycloaddition (cyclodimerization) was first observed more than 30 years ago, have now been observed. The additions of *N*-vinylcarbazole to both cyclopenta-1,3-diene and cyclohexa-1,3-diene, catalyzed by tris(4-bromophenyl)aminium hexachloroantimonate, have been observed. Further, a two step mechanism for these cycloadditions has been established through the use of stereospecifically labelled substrate ((*Z*)-*N*-(2-deuteriovinyl)carbazole).

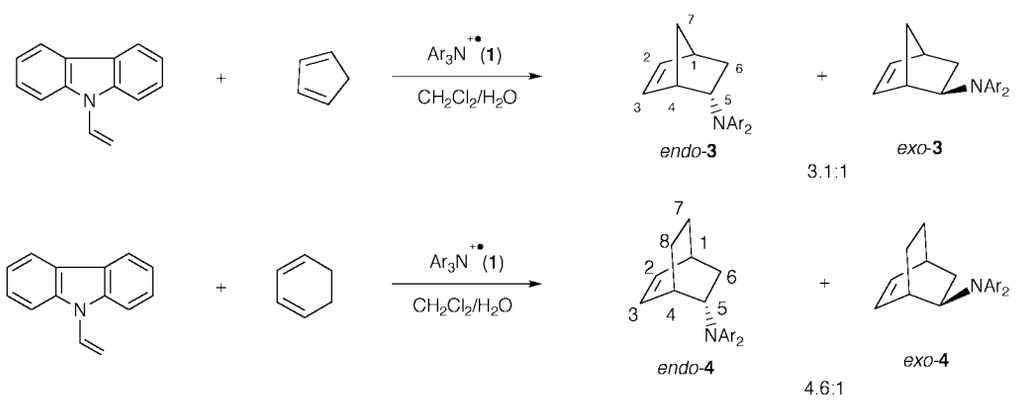
Introduction

The cyclodimerization of *N*-vinylcarbazole, reported 30 years ago, represented not only the first example of a radical cation/neutral cycloaddition reaction, but also the prototype example of a radical cation chain mechanism.[1,2] Although the field of radical cation cycloadditions has developed rapidly since that time,[3,4] no other examples of radical cation cycloadditions of *N*-vinylcarbazole to other neutral substrates seem to have been observed.[5] Using the tris(4-bromophenyl)aminium hexachloroantimonate salt (**1**) of Walter[6] and a modification of the methods for radical cation cycloadditions previously developed in this laboratory,[7] it has proved possible to effect radical cation Diels–Alder additions of *N*-vinylcarbazole (**2**) to both cyclopenta-1,3-diene and cyclohexa-1,3-diene. The mechanism of the reaction of **2** with cyclopenta-1,3-diene has been investigated by means of a stereospecifically deuterium-labelled version of **2**.

Results and discussion

The cyclodimerization of *N*-vinylcarbazole has been shown by the Ledwith group to occur efficiently when this substrate is treated with ferric ion in methanol or under photochemical electron transfer conditions, using chloranil (2,3,5,6-tetrachlorobenzo-1,4-quinone) as the sensitizer.[1,2] However, treatment with the aminium salt catalyst (**1**) typically used in this laboratory for inducing radical cation cycloadditions fails to generate more than traces of the cyclobutadimer of **2**, presumably because of competing acid-catalyzed, carbocation-mediated polymerization of **2**. Recently, a simple but valuable technique for minimizing acid-catalyzed side reactions under aminium salt conditions, which consists of using a two-phase water/methylene chloride solvent system instead of just methylene chloride, has been developed in this laboratory.[7] The use of water as a second phase was designed to remove any inorganic acid, which may initially have been present in the aminium salt catalyst, and also to continue to extract these acids from the methylene chloride solution as they are formed. Since **1** is rather insoluble in water and since the typical radical cation cycloaddition reactions are complete within 1–3 minutes or even less, reaction efficiency is diminished only moderately by the presence of water. Thus, instead of the more usual 5–10 mol% of catalyst, it is usually desirable to use *ca.* 20 mol% of **1** relative to **2**. When this modified reaction system is used in conjunction with **1** as the catalyst/initiator, the cyclodimer of *N*-vinylcarbazole could be obtained in low yields. This result was nevertheless encouraging enough to suggest the possible application of the new solvent/catalyst system in the search for radical cation Diels–Alder additions of **2** which, in our hands, could not be achieved under the classic ferric ion–methanol conditions.

The reaction of **2** with a ten-fold excess of cyclopenta-1,3-diene, catalyzed by **1**, in dichloromethane (in the absence of the aqueous phase) yielded, as expected, at most, traces of Diels–Alder adducts. However, when the two phase solvent system was used, a mixture of *endo*- and *exo*-Diels–Alder adducts (*endo*- and *exo*-**3**) was obtained in 30% yield, from which the individual pure adducts could be isolated in a 25% total yield (the sum of the yields of both adducts; Scheme 1). As has previously been found for other radical cation Diels–Alder cycloadditions, the *endo* isomer was found to be predominant

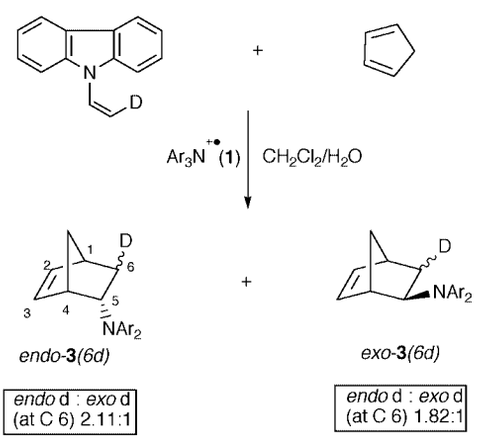


Scheme 1 Radical cation Diels–Alder cycloadditions of *N*-vinylcarbazole. Note that NAr_2 is used to succinctly symbolize the carbazolyl moiety.

(3.1 : 1). The analogous reaction with cyclohexa-1,3-diene similarly generated a Diels–Alder adduct mixture from which the pure adducts could be isolated in a total 25% yield (*endo* : *exo* = 4.6).

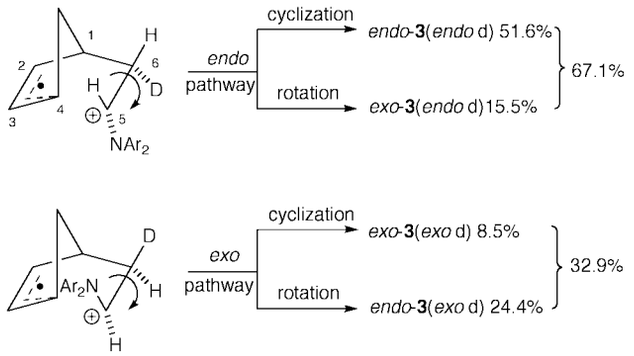
Reaction stereochemistry

The cyclodimerization of *N*-vinylcarbazole was originally proposed to occur *via* a stepwise mechanism involving a distonic radical cation intermediate. Stereochemical studies in this laboratory have recently provided strong support for a stepwise mechanism for this reaction,[8] although in contrast the radical cation cyclodimerization of *trans*-anethole (*p*-propenylanisole) has been found to be stereospecific and it has been suggested, based upon this[9,10] and other observations,[11] to be a concerted process. The stereochemistry of radical cation Diels–Alder additions is also of current interest. Several examples of stereospecific additions of this type have been reported,[12,13] but an example of a non-stereospecific reaction has also been reported very recently.[7] It therefore was of interest to determine the stereochemistry of a Diels–Alder addition of **2** as a criterion of the concerted or stepwise nature of the cycloaddition mechanism. The reaction with cyclopenta-1,3-diene was therefore studied using the stereospecifically deuterium labelled (*Z*)-*N*-(2-deuteriovinyl)carbazole (Scheme 2). In fact, it proved possible to determine the stereochemistry of the reactions which form both the *endo* and *exo* isomers of **3**, and the results in the case of the *exo* diastereoisomer are somewhat surprising. The deuterated substrate (**2**-*z*-d) was prepared by the *trans* stereospecific lithium aluminum deuteride reduction of *N*-ethynylcarbazole[14] and reacted with a 10-fold excess of cyclopenta-1,3-diene under the modified aminium salt conditions. The *endo* or *exo* position of the deuterium in both the *endo* and *exo* Diels–Alder diastereoisomers was determined by NMR spectroscopy on both the mixture of adducts and the individually purified adducts. This analysis was made feasible by the circumstance that the *endo* and *exo* protons at C6 of both the *endo* and *exo* (undeuterated) adducts (**3**) are well separated in their chemical shifts and are unambiguously identified by their NOESY spectra. In the *endo* adduct, the ratio of *exo* : *endo* C6 protons is found to be 2.11 : 1, while in the *exo* adduct the ratio of *exo* : *endo* C6 protons is 1.82 : 1.



Scheme 2 Stereochemistry of the radical cation Diels–Alder cycloaddition of *N*-vinylcarbazole to cyclopenta-1,3-diene.

Since a stereospecific reaction of **2**-*z*-d should give only *exo* C6 protons in the *endo* adduct and only *endo* C6 protons in the *exo* adduct, it is clear that the cycloaddition is non-stereospecific, strongly suggesting that the cycloaddition is stepwise (Scheme 3). The circumstance that the *endo* isomer has an excess of *exo* protons is, of course, to be expected from a predominantly suprafacial addition, but the result that the *exo* isomer also has an excess of *exo* protons reveals that this



Scheme 3 Cyclization and rotation of the diastereoisomeric distonic radical cations formed by *endo* and *exo* pathways.

product is formed predominantly *via* antarafacial cycloaddition. This interesting result is nicely rationalized, however, in terms of a stepwise mechanism in which C1–C6 bond formation occurs preferentially *via* an *endo* route, *i.e.*, in which the carbazolyl group (and the deuterium label) are initially *endo* oriented. Such an intermediate can either cyclize to give the *endo* adduct with *endo* deuterium (the predominant process) or, after rotation around the bond which will be the C5–C6 bond in the adduct, to give the *exo* adduct with *endo* deuterium. The latter process results in net antarafacial addition to the substrate. That this indirect route for forming the *exo* adduct is the predominant route may initially seem somewhat surprising, since it would appear plausible that more of the *exo* adduct would be formed by a direct *exo* approach. However, this apparent anomaly can be readily explained by postulating that, first of all, the *endo* approach is favored and, additionally, that the distonic radical cation formed by the *exo* approach also prefers to form the *endo* adduct by rotation around the C5–C6 bond, thus giving rise to relatively smaller amounts of the *exo* adduct. These assumptions appear reasonable if, in the distonic radical cation intermediate, the *endo* diastereoisomer is somewhat more stable than the *exo* diastereoisomer or if the *endo* diastereoisomer of the adduct radical cation (or the transition state leading to it) is more stable than the *exo*. These results further suggest that not only is the cycloaddition a stepwise one, but that the intermediate distonic radical cations (two diastereoisomeric ones) have sufficiently long lifetimes to undergo very extensive rotation or even rotational equilibration. This conclusion appears to follow from the comparable *endo* : *exo* adduct ratios formed in the diastereoisomeric (*endo* and *exo*) pathways (Scheme 3). In the *endo* pathway, the *endo* : *exo* adduct ratio is 3.3, while in the *exo* pathway, the *endo* : *exo* adduct ratio is 2.9. Both the preference of the *N*-vinylcarbazole radical cation for stepwise Diels–Alder addition and the apparent fact that the distonic radical cation intermediate is relatively long-lived seem eminently plausible in view of the ability of the amine function of the carbazole moiety to provide especially strong stabilization for the carbocationic moiety.

Interestingly, even though these Diels–Alder additions are stepwise processes, no evidence was found for the formation of cyclobutane adducts. Thus the signficant *endo diastereoselectivity* of the cycloaddition is complemented by an even stronger *Diels–Alder periselectivity*.

Experimental

General experimental conditions and equipment

Proton NMR spectra were recorded on a Bruker AC250 or a Varian UNITY INOVA 500 spectrometer. Carbon NMR spectra were recorded on the Bruker AC250 machine. COSY and NOESY spectra were recorded on the Varian UNITY INOVA 500 spectrometer. High resolution mass spectra were recorded on a VG ZAB-2E mass spectrometer. All chemicals used as

starting materials were purchased from the Aldrich Company and used as received. The dichloromethane solvent was dried by refluxing it over phosphorus pentoxide.

Reaction of *N*-vinylcarbazole (2) with cyclopenta-1,3-diene

A solution of 1.0 g (5.72 mmol) of **2** and 6.83 g (103.5 mmol) of cyclopenta-1,3-diene in 20 mL of dichloromethane was added to 0.845 g (1.035 mmol) of tris(4-bromophenyl)aminium hexachloroantimonate (**1**) in 120 mL of dichloromethane and 25 mL of water at 0–5 °C. The mixture was stirred for about 5 s and then quenched with an excess of a saturated solution of potassium carbonate in methanol, followed by the addition of water. The dichloromethane phase was separated, dried with sodium sulfate, and the solvent removed by rotary evaporation. The crude product was initially chromatographed on alumina (petroleum ether–dichloromethane, 13 : 1) to remove the triarylamine and other impurities and afford a mixture of *endo* and *exo* adducts (0.409 g, 30.5% yield, *endo* : *exo* = 3.1 : 1). The individual diastereoisomers were then isolated by chromatography on silica gel (petroleum ether–dichloromethane, 15 : 1), yielding 100 mg of *endo*-**3** and 10 mg of *exo*-**3**.

***endo*-3.** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.64–1.65 (q, 2H, *syn* and *anti* C7-H), 2.29–2.34 (td, 1H, J = 9.65, 3.62, C6-*exo*-H), 2.49–2.52 (m, 1H, C6-*endo*-H), 3.19 (s, 1H, C1-H), 3.46–3.47 (br s, 1H, C4-H), 5.30–5.34 [dt, J = 9.45 (d), 4.02 (t), 1H, C5-H], 6.00–6.01 (dd, J = 5.70, 2.85, 1H, C3-H), 6.61–6.63 (dd, J = 5.80, 3.09, 1H, C2-H), 7.20–7.23 (td, J = 7.54, 1.0, 2H), 7.38–7.42 (td, J = 7.24, 1.41, 2H), 7.54–7.56 (d, J = 8.45, 2H), 8.07–8.10 (m, 2H); ^{13}C NMR (CD_3Cl, 250 MHz) δ 28.24, 43.44, 48.36, 49.04, 57.53, 111.82, 118.63, 119.86, 123.40, 125.20, 134.11, 138.88, 140.88; HRMS *m*/*z* calcd. for $C_{19}H_{18}N$ (M + 1) 260.143925; found 260.143823.

***exo*-3.** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.90–1.93 (dt, J = 8.85, 1.81, 1H, *anti*-C7-H), 2.21–2.23 (d, J = 8.84, 1H, *syn*-C7-H), 2.04–2.09 (dt, J = 8.65, 2.01, 1H, *endo*-C6-H), 2.13–2.17 (m, 1H, *exo*-C6-H), 3.12 (s, 1H, C1-H), 3.68–3.69 (br s, 1H, C4-H), 4.56–4.58 (ddd, J = 8.02, 4.0, 1.4, 1H, C5–H), 6.29–6.30 (dd, J = 5.63, 3.22, 1H, C3-H), 6.40–6.41 (dd, J = 5.83, 2.82, 1H, C2-H), 7.23–7.26 (td, J = 7.54, 1.0, 2H, aromatic), 7.42–7.46 (td, J = 7.84, 1.40, 2H, aromatic), 7.55–7.57 (m, 2H, aromatic), 8.11–8.13 (m, J = 7.24, 0.81, 2H, aromatic); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 32.574, 40.759, 46.706, 48.309, 58.348, 110.835, 118.700, 120.038, 123.592, 125.540, 135.063, 140.155, 140.450; HRMS *m*/*z* calcd. for $C_{19}H_{18}N$ (M + 1) 260.143925; found 260.144517.

The *endo* and *exo* adducts of **3** were both subjected to 500 MHz NOESY spectroscopy in order to assign all protons and especially to identify with certainty the *endo*- and *exo*-C6 protons. The *exo*-C6 proton of *endo*-**3** was characterized by a strong interaction with the *syn*-C7 proton, whose interaction was lacking in the *endo*-C6 proton. The *exo*-C6 proton also has a much stronger interaction with the C5 proton (which is also *exo*), than does the *endo*-C6 proton. Further, the *endo*- but not the *exo*-C6 proton interacts strongly with the C2 olefinic proton. In *exo*-**3**, similar strong interactions between the *exo*-C6 proton with the *syn*-C7 proton are observed, which are conspicuously absent for the *endo*-C6 proton are observed. Again, the *endo*-C6 proton interacts selectively with the olefinic proton at C2. All criteria are in agreement with the proposed assignment.

Reaction of *N*-vinylcarbazole with cyclohexa-1,3-diene

A solution of 200 mg (1.035 mmol) of **2** and 828 mg of cyclohexa-1,3-diene in 5 mL of dichloromethane was added to 20 mL of water and 80 mL of dichloromethane containing 169 mg of **1** at 0 °C. After stirring for 5 s, the reaction mixture was quenched with an excess of a saturated solution of potassium carbonate in methanol. After addition of more water, the organic phase was separated, washed with water, dried over sodium sulfate, and the solvent removed by rotary evaporation. The crude product was purified by silica gel chromatography (petroleum ether–dichloromethane, 10 : 1) to give 55 mg (19.5%) of the *endo* adduct and 20 mg (7.1%) of the *exo* adduct. The latter adduct was especially difficult to purify completely, and is incompletely characterized.

***endo*-4.** ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.37–1.47 (m, 2H, C7, *anti*-C8), 1.66–1.71 (m, 1H, *syn*-C7), 1.91–1.96 (m, 1H, *syn*-C8), 2.13–2.19 (dt, J = 11.96, 2.82, 1H, *exo*-C6), 2.47–2.52 (m, 1H, *endo*-C6), 2.83–2.87 (m, 1H, C4-H), 2.91–2.92 (m, 1H, C1-H), 4.94–4.98 (ddd, J = 10.26, 6.03, 2.01, 1H, C5-H), 6.30–6.33 (t, J = 7.24, 1H, C3-H), 6.65–6.68 (dt, J = 7.44, 1.00, 1H, C2-H), 7.18–7.21 (td, J = 7.34, 1.01, 2H, aromatic), 7.37–7.41 (td, J = 7.84, 1.21, 2H, aromatic), 7.58–7.59 (d, J = 8.25, 2H, aromatic), 8.06–8.08 (m, 2H, aromatic); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 23.675, 26.313, 30.347, 30.828, 36.552, 55.394, 111.639, 118.554, 119.945, 123.378, 125.070, 133.285, 134.966, 140.063; HRMS *m*/*z* calcd. for $C_{20}H_{20}N$ (M + 1) 274.159575, found: 274.159471.

***exo*-4.** The NMR spectrum of the minor diastereoisomer, which could not be isolated in very pure form, was very similar to that of the major one in the upfield region. It is especially distinguished by the absorption of the C5 proton at 4.66–4.70 (m), and the C2, C3 olefinic protons at δ 6.49 (m).

Preparation of (*Z*)-*N*-(2-deuteriovinyl)carbazole

Lithium aluminum deuteride (168 mg, 3.92 mmol) was dissolved in freshly distilled tetrahydrofuran (4 mL), and 9-ethynylcarbazole (765 mg, 4 mmol) dissolved in 2 mL of anhydrous tetrahydrofuran was added dropwise, with stirring, over a 10 minute period into the solution of the deuteride reagent. Stirring was continued for 60 minutes at room temperature, followed by addition of dilute hydrochloric acid, extraction with dichloromethane, drying with anhydrous sodium sulfate, filtration, and evaporation of the solvent by rotary evaporation. The product (712 mg, 92%), was obtained as a light pink solid: mp 64–65 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 5.13 (d, J = 9.09, 1H, vinyl proton *trans* to carbazolyl group), 7.25–8.08 (m, 9H); ^{13}C NMR ($CDCl_3$, 250 MHz) δ 102, 110.4, 120.2, 120.6, 124.1, 126.2, 130.0, 139.2; LRMS(CI) *m*/*z* 195 (M + 1); HRMS(CI) *m*/*z* calcd. for $C_{14}H_{11}DN$ 195.103251; found 195.102637.

Reaction of (*Z*)-*N*-(2-deuteriovinyl)carbazole with cyclopenta-1,3-diene

A solution of the deuterated *N*-vinylcarbazole (>98% *z*-deuterio; 100 mg, 0.515 mmol) and 478 mg of cyclopenta-1,3-diene in 5 mL of dichloromethane were added to **1** (59 mg) in dichloromethane (25 mL) and water (6 mL) at 0–5 °C. The reaction mixture was quenched after 5 s as previously, washed with water, the aqueous phase extracted with more dichloromethane, and the combined dichloromethane extracts dried and the solvent evaporated by rotary evaporation. The crude mixture was purified on an alumina column using petroleum ether–dichloromethane (15 : 1) to give 5 mg of the pure *endo* adduct and 32 mg of a mixture of the *endo* and *exo* adducts (total yield, 23%). The latter mixture was further purified by silica gel chromatography to give 2 mg of the *exo* isomer, another 10 mg of the pure *endo* isomer, and 12 mg of a mixture. The individual diastereoisomers were characterized by comparison of the proton NMR spectra with the undeuterated adducts and by HRMS. *endo*-**3** (6-deuterio): HRMS (M + 1) calcd. for $C_{19}H_{17}DN$ 261.150201; found 261.150383. *exo*-**3** (6-deuterio): HRMS (M + 1) calcd. for $C_{19}H_{17}DN$ 261.150201, found 261.151975. The percentages of *endo* and *exo* protons in both adduct

diastereoisomers was then determined by integration of the 250 MHz COSY spectra.

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References

1 F. A. Bell, R. A. Crellin, H. Fuji and A. Ledwith, *J. Chem. Soc.*, *Chem. Commun.*, 1969, 251.
2 R. A. Crellin, M. C. Lambert and A. Ledwith, *J. Chem. Soc.*, *Chem. Commun.*, 1979, 682; A. Ledwith, *Acc. Chem. Res.*, 1972, **5**, 133.
3 N. L. Bauld, *Tetrahedron*, 1989, **45**, 5307.
4 N. L. Bauld, *Advances in Electron Transfer Chemistry*, Vol. 2, Ed. P. S. Mariano, JAI Press, 1992, 1.
5 An inverse polarity (Umpolung) Diels–Alder addition of neutral *N*-vinylcarbazole has, however, been suggested, but the product was apparently not structurally characterized: C. K. Bradsher, G. L. B. Carlson, N. A. Porter, I. J. Westerman and T. J. Wallis, *J. Org. Chem.*, 1978, **43**, 822; I. J. Westerman and C. K. Bradsher, *J. Org. Chem.*, 1979, **44**, 727.
6 R. I. Walter, *J. Am. Chem. Soc.*, 1966, **88**, 1923.
7 N. L. Bauld and J. Yang, *Tetrahedron Lett.*, 1999, **40**, 8519.
8 N. L. Bauld and D. Gao, *J. Chem. Soc.*, *Perkin Trans. 2*, in the press.
9 N. L. Bauld and R. Pabon, *J. Am. Chem. Soc.*, 1983, **105**, 633.
10 F. D. Lewis and M. Kojima, *J. Am. Chem. Soc.*, 1988, **110**, 8660.
11 N. P. Shepp, D. Shukla, H. Sarker, N. L. Bauld and L. J. Johnston, *J. Am. Chem. Soc.*, 1997, **119**, 10325.
12 D. J. Bellville, D. D. Wirth and N. L. Bauld, *J. Am. Chem. Soc.*, 1981, **103**, 718.
13 N. L. Bauld and J. Yang, *Org. Lett.*, 1999, **1**, 773.
14 J. Pielichowski and R. Chrzaszcz, *Bull. Soc. Chim. Belg.*, 1994, **104**, 117; M. Hojo, R. Masuda and S. Takagi, *Synthesis*, 1978, **4**, 284.

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