The development of strong covalent interactions in inner sphere electron transfer reactions between cation radicals and neutral molecules

Nathan L. Bauld, J. Todd Aplin, Wang Yueh, Angie Loving and Stephanie Endo

Department of Chemistry and Biochemistry, The University of Texas, Austin, TX 78712, USA

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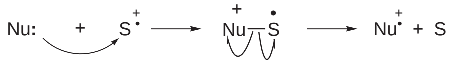
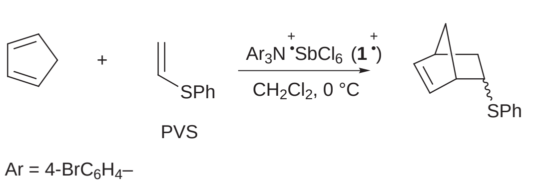
The cation radical Diels–Alder reactions of a series of *meta* and *para* substituted aryl *cis*-prop-1-enyl ethers with 2,3-dimethylbuta-1,3-diene catalyzed by tris(4-bromophenyl)aminium hexachloroantimonate have been studied mechanistically. The reactions are found to occur primarily *via* an indirect route involving cation radical cyclobutanation followed by cation radical vinylcyclobutane rearrangement. Kinetic studies reveal that the ionization of these ethers to the corresponding cation radicals occurs by an inner sphere mechanism.

Cation radicals of a variety of ionizable substrates can be conveniently generated in solution by electron transfer to (equivalent to hole transfer *from*) triarylaminium salts. This convenient method for cation radical generation has been used to develop and study a wide range of cation radical pericyclic chemistry including Diels–Alder addition, cyclobutanation, cyclopropanation, polymerization, and vinylcyclobutane rearrangement.[1,2] Attention has recently focused upon the *mechanism* of the electron (hole) transfer reaction between aminium ions and substrate molecules.[3–9] Conventionally, electron transfer (ET) processes are classified as *outer sphere* (*i.e.* involving no significant covalent interaction between the donor and acceptor) or *inner sphere* (*i.e.*, involving significant covalent interaction between the donor and acceptor). Recently, this research group has postulated, and found evidence to support, an electron transfer process which involves electrophilic attack by the aminium salt upon the neutral substrate, followed by homolysis of the newly formed covalent bond (Scheme 1).[10–12]

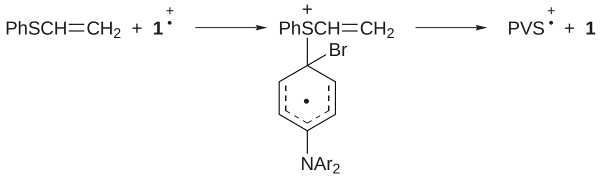


Scheme 1 The polar mechanism for electron (hole) transfer.

This *polar* mechanism for overall ET can be considered to be a limiting form of inner sphere ET. An especially important precedent for the present work is the Diels–Alder reaction of phenyl vinyl sulfide (PVS) with cyclopenta-1,3-diene (Scheme 2).[10,11] That this Diels–Alder addition involves the phenyl vinyl sulfide cation radical ($PVS^{\cdot+}$) as the reactive dienophile has been rigorously established by a wide variety of evidence, including the generation of the same adducts in virtually identical *endo* : *exo* ratios when the PVS cation radical is generated by anodic oxidation and by photosensitized electron transfer. The rate determining step of the overall reaction was found to be the reaction between the aminium salt ($\mathbf{1}^{\cdot+}$) and PVS, thus permitting the mechanism of this ET process to be probed kinetically. Importantly, the transition state for the rate determining reaction of $\mathbf{1}^{\cdot+}$ with PVS was found to have little, if any, cation radical character on the PVS moiety but instead to involve exceptionally strong covalent bonding of $\mathbf{1}^{\cdot+}$, as an electrophile, to PVS as a nucleophile (Scheme 3). Stereochemical studies further suggested that the electrophilic attack of $\mathbf{1}^{\cdot+}$ occurs primarily on sulfur, as opposed to the β vinyl carbon atom. The present research was designed to probe the generality of this novel polar mechanism of ET in the reactions of triarylaminium salts with electron rich alkenes. More specifically, it was of special interest to see whether the polar mechanism would still be operative if the nucleophilic sulfur atom were replaced by a much less nucleophilic oxygen atom.



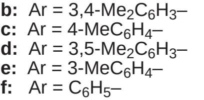
Scheme 2 Cation radical Diels–Alder reaction of phenyl vinyl sulfide with cyclopenta-1,3-diene.



Scheme 3 Mechanism of the reaction of the phenyl vinyl sulfide cation radical with $\mathbf{1}^{\cdot+}$.

Results and discussion

A series of eight *m*- and *p*-substituted aryl *cis*-prop-1-enyl ethers (**2a**–**h**; Scheme 4) was synthesized by reacting the appropriate aryloxide anion with allyl bromide, and then rearranging the resulting allyl aryl ethers to the propenyl ethers



2a–h

3 (*trans* > *cis*)

2a: Ar = 4-MeOC$_6$H$_4$–
2b: Ar = 3,4-Me$_2$C$_6$H$_3$–
2c: Ar = 4-MeC$_6$H$_4$–
2d: Ar = 3,5-Me$_2$C$_6$H$_3$–
2e: Ar = 3-MeC$_6$H$_4$–
2f: Ar = C$_6$H$_5$–
2g: Ar = 4-BrC$_6$H$_4$–
2h: Ar = 3-ClC$_6$H$_4$–

Scheme 4 Reaction of aryl *cis*-prop-1-enyl ethers with 2,3-dimethylbuta-1,3-diene.

Table 1 Relative rates of cycloaddition of aryl *cis*-prop-1-enyl ethers to 2,3-dimethylbuta-1,3-diene, catalyzed by tris(2,4-dibromophenyl)aminium hexachloroantimonate at 0 °C in dichloromethane

Substituent	Compound	log k_{rel}
4-Methoxy	**2a**	1.025
3,4-Dimethyl	**2b**	0.942
4-Methyl	**2c**	0.640
3,5-Dimethyl	**2d**	0.472
3-Methyl	**2e**	0.300
H	**2f**	0.000
4-Bromo	**2g**	−1.050
3-Chloro	**2h**	−2.090

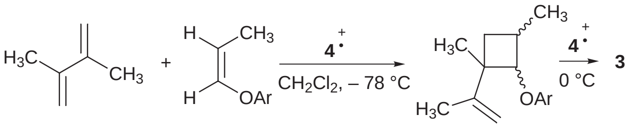
in base.[13] The propenyl ether products contained less than 2% of the corresponding *trans* isomers. Diels–Alder additions of these ethers with 2,3-dimethylbuta-1,3-diene catalyzed by triarylaminium salts were then studied (0 °C, dichloromethane). The reactions of all of these ethers except those having *para* electron donor substituents (**2a**–**c**) were found to be extremely slow when tris(4-bromophenyl)aminium hexachloroantimonate ($\mathbf{1}^{\cdot+}$) was used as the catalyst. Although this range of substrates was not sufficient for a definitive kinetic study of substituent effects, the Diels–Alder adducts generated from **2b** could be readily isolated and were fully characterized. Interestingly, the reaction proves to be non-stereospecific, the *cis* and *trans* adducts being formed in comparable amounts (*trans*: *cis* ≈ 2 : 1). Equally interestingly, the recovered propenyl ether is not isomerized at all, but instead retains the original 98 : 2 *cis* : *trans* ratio.

Kinetic and stereochemical studies

The more powerful aminium salt tris(2,4-dibromophenyl)aminium hexachloroantimonate ($\mathbf{4}^{\cdot+}$) was then selected as a catalyst which would potentially be capable of effecting the ionization of all eight substrates. This proved to be the case, and relative rates of reaction of all of these substrates with 2,3-dimethylbuta-1,3-diene were measured by competition kinetics as described in several previous publications.[3–11] The data are presented in Table 1. The preference for correlation with Hammett σ as opposed to σ^+ values is extraordinarily clear and is statistically valid at even the 99% confidence level. Indeed, the statistical validity of the preference for the correlation with σ is retained even when the point for the 4-methoxy substituent is omitted. The exceptionally well defined preference for the σ correlation is further evident when the points for the *meta* substituents (for which σ and σ^+ are equal) are permitted to define the regression line. The points for substrates having *para* substituents all fall quite close to the *meta* regression line when the σ parameters are used, but deviate grossly when σ^+ parameters are used. As was the case for $\mathbf{1}^{\cdot+}$ as catalyst, these reactions are all non-stereospecific and show a modest preference for the *trans* Diels–Alder adduct as revealed by the 500 MHz ^{1}H NMR spectra of the adducts (Scheme 6). Also as with $\mathbf{1}^{\cdot+}$, the unreacted portions of the *cis*-propenyl ethers are recovered stereochemically intact after the reactions.

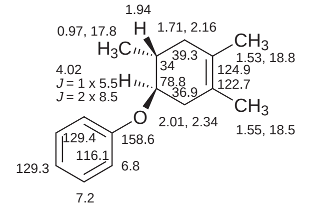
Direct *vs.* indirect Diels–Alder

In the course of the kinetic studies using $\mathbf{4}^{\cdot+}$ as the catalyst, the clean formation of the Diels–Alder adducts (*cis*- and *trans*-**3**) was established in each case. In particular, no other adducts, cyclic or acyclic, were found in significant amounts. Since cation radical cyclobutanation is also typically a very facile process,[1] the exclusive formation of Diels–Alder adducts drew our attention. This was especially the case because in a number of reported instances vinyl ethers, in particular, have been shown to exhibit a strong tendency to add to *acyclic* dienes *via* an admixture of Diels–Alder and cyclobutanation modes, with cyclobutanation often being the preferred mode.[14] Furthermore, the *non-stereospecific* formation of the Diels–Alder adducts appeared suspicious, since direct Diels–Alder reactions studied in this laboratory have proved to be stereospecific.[15] Finally, this group has previously observed *indirect* cation radical Diels–Alder (DA) reactions, which involve cation radical cyclobutanation (CB) followed by cation radical vinylcyclobutane (VCB) rearrangement.[16] The latter rearrangements are, in some cases, found to be non-stereospecific. Consequently the reaction of the unsubstituted propenyl ether (**2f**) was studied at −78 °C, at which temperature the cation radical VCB rearrangement was expected to be slowed sufficiently to observe the intermediate CB products. Indeed, when this reaction was carried out at −78 °C for short reaction times, CB adducts were observed in large amounts (CB : DA as high as 2 : 1; Scheme 5).

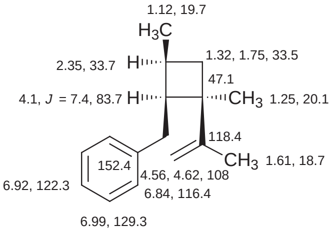


Scheme 5 The indirect path for cation radical Diels–Alder cycloaddition.

Three such CB adducts are formed in the ratio 7.2 : 1.5 : 1. These compounds were characterized by their ^{1}H and ^{13}C NMR spectra (Scheme 6), their retrocyclic fragmentation patterns in the mass spectrometer and by their subsequent efficient conversion at 0 °C in the presence of $\mathbf{4}^{\cdot+}$ to **3** (Scheme 5). Interestingly, the ratio of *trans*: *cis* **3** increases from 2.8 : 1 to 3.9 : 1 subsequent to the rearrangement. Evidently the VCB rearrangement is a stepwise, non-stereospecific process which favors the more stable, *trans* isomer of **3**. The relatively larger amount of *cis*-**3** which is formed in the reaction at −78 °C might then result from a contribution from the stereospecific direct Diels–Alder addition.



Major Diels-Alder Adduct (*trans*)

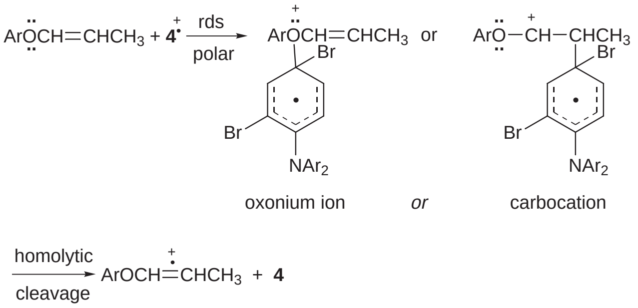


Major Cyclobutane Adduct

Scheme 6 ^{13}C and ^{1}H NMR chemical shifts of the major Diels–Alder and cyclobutane adducts.

Mechanism of the substrate ionization step

Experimental studies have previously demonstrated that the one electron oxidation of *m*- and *p*-substituted aryl propenyl ethers and also aryl vinyl sulfides to the corresponding cation radicals correlates extremely well with the Brown σ^+ parameters.[10,12] The correlation with Hammett σ values is far inferior and the preference for the σ^+ correlation is found to be statistically significant at the 95% confidence level in both reaction series. *Ab initio* and semi-empirical calculations of the gas phase ionization energies of aryl vinyl ethers were also found to correlate preferentially with σ^+. In sharp contrast, electrophilic additions to these same electron rich substrates at either the β vinyl carbon, to yield an α-aryloxy- or α-arylthio carbocation, or at the heteroatom, to yield an 'onium ion, have been shown by numerous experimental and theoretical studies to correlate preferentially and statistically significantly with σ. The extremely good correlation of the rates of reaction of $\mathbf{4}^{\cdot+}$ with **2a**–**h** with σ and the very poor correlation with σ^+ indicate that the transition state for this reaction has developed little or no cation radical character upon the substrate moiety. Since the large, negative ρ value for the reaction indicates a substantial build-up of positive charge upon the substrate, it follows that the transition state for this reaction is best described as having a high degree of either *oxonium* or *carbocation* character (Scheme 7). An experimental distinction between these two closely related reaction modes cannot as yet be made decisively.



Scheme 7 Mechanism of the reaction of **2** with $\mathbf{4}^{\cdot+}$.

Summary

The Diels–Alder reactions of a series of either *m*- or *p*-substituted aryl *cis*-prop-1-enyl ethers with 2,3-dimethylbuta-1,3-diene catalyzed by tris(2,4-dibromophenyl)aminium hexachloroantimonate ($\mathbf{4}^{\cdot+}$) at 0 °C are non-stereospecific and occur primarily *via* an indirect Diels–Alder reaction. When the reaction is carried out at −78 °C, the vinylcyclobutane adducts are readily observed, and these are efficiently converted to the Diels–Alder adducts when the reaction temperature is raised to 0 °C. This cation radical vinylcyclobutane rearrangement is non-stereospecific, thus accounting for the formation of a *cis*/*trans* mixture of Diels–Alder adducts. The correlation of the relative rates of ionization of these substrates by $\mathbf{4}^{\cdot+}$ with Hammett σ values in a strong and statistically significant preference to Brown σ^+ values establishes that the transition state for this overall electron transfer process has little or no cation radical character upon the substrate moiety. The very extensive development of positive charge upon the substrate, as indicated by the large, negative ρ value, is consistent with either carbocation or oxonium ion character. Consequently, an inner sphere electron transfer mechanism involving strong covalent (electrophilic) attachment to the substrate (*via* oxygen or carbon) is indicated.

Experimental

Analysis

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 250 spectrometer as solutions in $CDCl_3$. Chemical shifts (δ) are reported in parts per million downfield from the reference, tetramethylsilane. High field ^{1}H NMR spectra were recorded on a General Electric GN-500 spectrometer. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; dtd, triplet of doublets; m, multiplet. Analytical gas chromatographic (GC) analyses were performed on a Perkin-Elmer Model 8500 instrument using a PE Nelson Model 1020 reporting integrator for data collection. The instrument was equipped with flame ionization detectors and a DB-1 (J&W Scientific) capillary column (30 m × 0.25 mm id, 1 µm film thickness) using helium as the carrier gas. Dodecane was used as the internal standard for all of the quantitative analyses. Low resolution mass spectrometry was performed on a Hewlett-Packard Model 5971A GC-MS spectrometer equipped with a DB-1 capillary column (15 m × 0.25 mm id, 1 µm film thickness).

Solvents and reagents

Methylene chloride and acetonitrile were dried over phosphorus pentoxide. Hexane was dried over calcium hydride. Tris(4-bromophenyl)aminium hexachloroantimonate ($\mathbf{1}^{\cdot+}$) was purchased from Aldrich. The corresponding hexabromo salt ($\mathbf{4}^{\cdot+}$) was synthesized *via* a literature procedure.[17] The synthesis of the aryl propenyl ethers has previously been reported.[12] The kinetic methods for obtaining relative rate constants have been described in a series of papers.[3–12]

Reaction of 3,4-dimethylphenyl *cis*-prop-1-enyl ether (2b) with 2,3-dimethylbuta-1,3-diene, catalyzed by $\mathbf{1}^{\cdot+}$

To an ice-cooled 50 mL round bottom flask equipped with a magnetic stirrer and nitrogen inlet and containing 18.5 mL of anhydrous dichloromethane was added 3,4-dimethylphenyl *cis*-prop-1-enyl ether (0.196 g, 1.21 mmol), followed by 2,3-dimethylbuta-1,3-diene (0.645 g, 7.85 mmol), and then the catalyst, tris(4-bromophenyl)aminium hexachloroantimonate ($\mathbf{1}^{\cdot+}$; 0.077 g, 7.8 mol% based upon the propenyl ether). The mixture was stirred for ten minutes at 0 °C, at which time the reaction was quenched with 2 mL of K_2CO_3–CH_3OH. Dichloromethane (100 mL) was added to the solution and the organic layer was extracted with water (3 × 100 mL). The resulting organic solution was dried over $MgSO_4$ and the solvent removed, affording 0.356 g of a clear oil. Chromatography on alumina (hexane eluent) gave 0.145 g (49%) of the adducts, following elution of the triarylamine (**1**) and starting material (**2b**): ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, d, *J* 5.5 Hz, *cis* isomer), 0.95 (3H, d, *J* 5.4, *trans* isomer), 1.50 (3H, s), 1.55 (3H, s), 1.4–2.1 (4H, m), 2.09 (3H, s), 2.12 (3H, s), 2.3 (1H, m), 4.0 (1H, dt), 4.3 (1H, td), 6.6 (2H, m), 7.2 (1H, d); HRMS calc. for $C_7H_{24}O$ 244.182716; found 244.181573.

Reaction of phenyl *cis*-prop-1-enyl ether (2b) with 2,3-dimethylbuta-1,3-diene, catalyzed by $\mathbf{4}^{\cdot+}$ at −78 °C and the vinyl cyclobutane rearrangement of the cyclobutane adducts at 0 °C

To a 50 mL round bottom flask fitted with a nitrogen inlet, phenyl *cis*-prop-1-enyl ether (0.125 g, 0.933 mmol), 2,3-dimethylbuta-1,3-diene (0.311 g, 3.79 mmol) and 20 mL dichloromethane were added. The round bottom flask was placed in an acetone/dry ice bath at −78 °C, then $\mathbf{4}^{\cdot+}$ (0.115 g, 11%) was added as a solid. After 5 minutes, the reaction was quenched by the addition of 1 mL of saturated K_2CO_3 in methanol, washed with water (3 × 5 mL), dried over $MgSO_4$, and the solvent removed. GC analysis revealed that the ratio of recovered starting material to products was 1:1. GC–MS analysis showed that the product mixture consisted of 71% cyclobutane adducts as three isomers in a ratio of 7.2:1:1.4 and Diels–Alder adducts as two isomers in a ratio of 1:2.8. The product mixture was divided into two equal parts. The first part was dissolved in pentane and passed through a small plug of alumina. The solvent was removed on a rotary evaporator and 2D NMR analysis performed (see Scheme 6). The second part of the crude product mixture was dissolved in 10 mL dichloromethane at 0 °C and $\mathbf{4}^{\cdot+}$ (0.05 g) was added. After 5 minutes, the reaction was quenched and worked up as before. GC, GC–MS and 2D NMR analysis demonstrated that only the Diels–Alder adducts, in a ratio of 1:3.9, remained: *trans* Diels–Alder adduct, ^{1}H NMR δ 0.97 (d, 3H), 1.53 (s, 3H), 1.55 (s, 3H), 1.71

(m, 1H), 1.94 (m, 1H), 2.01 (m, 1H), 2.16 (m, 1H), 2.34 (m, 1H), 4.02 (dt, 1H, *J* 5.5, *J* 8.5), 6.8 (m, 2H), 7.2 (m, 3H); ^{13}C NMR δ 17.8, 18.5, 18.8, 34, 36.9, 39.3, 78.8, 116.1, 122.7, 124.9, 129.3, 129.4, 158.6; LRMS *m*/*e* 216 (M$^+$), 123 (base), 107, 81; *cis* Diels–Alder adduct, ^{1}H NMR δ 0.98 (d, 3H), 1.62 (s, 3H), 1.64 (s, 3H), 1.87 (m, 1H), 4.42 (dt, 1H, *J* 3.0, *J* 5.0), 6.8 (m, 2H), 7.2 (m, 3H); ^{13}C NMR δ 15.4, 33.7, 39.4, 76; LRMS *m*/*e* 216 (M$^+$), 123 (base), 107, 81; major cyclobutane adduct ^{1}H NMR δ 1.12 (d, 3H), 1.25 (s, 3H), 1.32 (m, 1H), 1.61 (s, 13H), 1.75 (m, 1H), 2.35 (m, 1H), 4.1 (d, 1H, *J* 7.4), 4.56 (s, 1H), 4.62 (s, 1H), 6.84 (m, 2H), 6.92 (m, 2H); ^{13}C NMR δ 18.7, 19.7, 20.1, 33.5, 33.7, 47.1, 83.7, 108, 116.4, 118.4, 122.3, 129.3, 152.4; LRMS *m*/*e* 216 (M$^+$), 180, 173, 159, 134 (base), 123, 105, 94, 77; first minor cyclobutane adduct, ^{1}H NMR δ 1.12 (d, 3H), 1.48 (m, 1H), 2.26 (m, 1H), 2.69 (m, 1H), 4.6 (d, 1H, *J* 7.8), 6.8 (m, 2H), 7.2 (m, 3H); ^{13}C NMR δ 15.6, 34.9, 78.9; LRMS *m*/*e* 216 (M$^+$), 180, 173, 134 (base), 123, 105, 94, 77; second minor cyclobutane adduct, ^{1}H NMR δ 1.1 (d, 3H), 2.38 (m, 1H), 4.05 (d, 1H, *J* 6.4), 6.8 (m, 2H), 7.2 (m, 3H); ^{13}C NMR δ 9.6, 36.8, 86.5; LRMS *m*/*e* 216 (M$^+$), 180, 173, 134 (base), 123, 105, 94, 77. Note: The NMR spectra of the minor isomers could not be completely assigned because of the weakness of the absorptions.

Acknowledgements

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