VOLUME 118, NUMBER 45
NOVEMBER 13, 1996

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Electron Transfer Photochemistry of Geraniol and (*E*,*E*)-Farnesol. A Novel "Tandem", 1,5-Cyclization, Intramolecular Capture

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Received July 31, 1995[⊗]

Abstract: The electron transfer photoreaction between 9,10-dicyanoanthracene (DCA) and (*E*)-3,7-dimethylocta-2,6-dien-1-ol (geraniol, (*E*)-**1**) in dichloromethane produces mainly *cis*-2-(2-propenyl)-*trans*-5-methylcyclopentanemethanol, *cis*,*trans*-**3**, whereas irradiation of acetonitrile solutions of 1,4-dicyanobenzene (DCB) and (*E*)-**1** forms mainly two *trans*-fused 3-oxabicyclo[3.3.0]octanes (**4**, R = H; **5**, R = *p*-C_6H_4CN). Analogous results are observed in the photoreaction of farnesol ((*E*,*E*)-**2**) with DCB in the presence of phenanthrene as cosensitizer. The photoreaction of DCB with **1** or **2** has sufficient driving force ($\Delta G = -0.7$ eV in acetonitrile) for the generation of solvent-separated radical ion pairs (SSRIPs); in contrast, the marginal driving force ($\Delta G \approx 0$ eV) of the DCA sensitized reaction allows only the formation of contact radical ion pairs (CRIPs). The resulting radical cations react by five-center C−C cyclization, yielding di-tertiary, 2,α-bifunctional methylidenecyclopentyl radical cations, *cis*- or *trans*-**B**$^{\bullet+}$. Subsequently, CRIPs undergo rapid back electron transfer and intramolecular hydrogen transfer, generating product **3**. The radical cations, *trans*-**B**$^{\bullet+}$, of SSRIPs undergo a second cyclization by intramolecular nucleophilic capture, generating 3-oxabicyclo[3.3.0]oct-6-yl free radicals, *trans*-**C**$^{\bullet}$.

Introduction

The structures and reactions of organic radical cations have been the focus of much interest for the past decade.[1] Among bimolecular reactions, their additions to alkenes[2] and their nucleophilic capture by alcohols,[3] which lead to C−C and C−O bond formation, respectively, have been investigated in detail. Among unimolecular reactions, geometric isomerizations[4] and several molecular rearrangements have attracted attention. For the electron transfer induced Cope rearrangement of 1,5-hexadiene systems, several mechanistic extremes have been established.[5] This reorganization may proceed via a "dissociative"[5b−d] or an "associative" mechanism.[5e] The respective intermediates, either bifunctional, doubly allylic radical cations[5b−d] or 1,4-cyclohexanediyl radical cations,[5e,6] have been characterized by CIDNP[5b−d] and/or ESR spectroscopy.[6] Several 1,4-diarylcyclohexane-1,4-diyl radical cations have been intercepted by superoxide ion, giving rise to the 2,3-dioxabicyclo-[2.2.2]octane system.[5e] The tendency toward 1,6-cyclizations suggested by these results[5e,6] stands in interesting contrast to the well-established photoreactions of nonconjugated dienes, whose reactions are rationalized via five membered ring biradicals as preferred intermediates ("rule of five");[7] nonconjugated alkenyl radicals also prefer five-center cyclizations.[8] Since the main difference between the excited states of nonconjugated dienes, on the one hand, and the corresponding radical cations, on the other, is the presence or absence of an electron in an antibonding orbital, one might have expected similar reactivity for the two types of intermediates.

Considering that the 1,6-cyclization of the 2,5-diarylhexadiene radical cations benefit from a stabilizing effect of the phenyl groups in the 1,4-diyl intermediate,[5e] we have begun to investigate electron transfer induced reactions of hexadiene

[⊗] Abstract published in *Advance ACS Abstracts*, November 1, 1996.

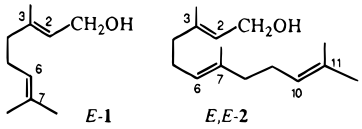
S0002-7863(96)02206-8 CCC: $12.00

Table 1. Product Yields in the Photoinduced Electron Transfer Reaction of Geraniol ((*E*)-**1**)[a]

sensitizer	solvent	ΔG_{et} (eV)[14]	*c,t*-**3**	*t,c*-**3**	*t,c*-**4**	*c,c*-**4**	*t,t*-**4** and *c,t*-**4**	*t,t*-**5**	*t,c*-**5**	*c,t*-**5**	(*Z*)-**1**
DCA	CH_2Cl_2	+0.1	70	6		6					13
DCA/BP	CH_2Cl_2		75	5	1	4	4				6
DCA	CH_3CN	−0.1	11		27		35				20
DCB	CH_2Cl_2	−0.5	25		4	6					60
DCB	CH_3CN	−0.7	4		15	2	9	12	17	17	4
DCB/Ph	CH_3CN				11		4	15	25	20	24

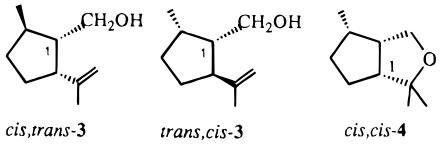
[a] Based on GC integration (H_2, FID detector).

systems without a strong built-in preference for 1,6-cyclization. We chose (*E*)-3,7-dimethylocta-2,6-dien-1-ol (geraniol, **1**) and (*E*,*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-ol (farnesol, **2**) as our initial targets. The substitution pattern of these systems (3,7-dimethyl) favors the formation of a five-membered ring, though the preference is less pronounced than in the 1,6-diphenyl derivatives. The hydroxy function present at C-1 represents an additional attractive feature of these systems; this function may serve as an intramolecular nucleophilic trapping site, either in competition with or subsequent to C−C cyclization. The results confirm that both **1** and **2** undergo several novel electron transfer induced intramolecular cyclization reactions.[9]

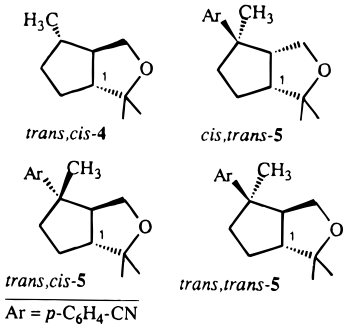


Results

The irradiation of 9,10-dicyanoanthracene (**DCA**) and (*E*)-**1** in methylene chloride produced 70% *cis*-2-isopropenyl-*trans*-5-methyl-1-cyclopentanemethanol (*cis*,*trans*-**3**), 6% *trans*,*cis*-**3**, and a bicyclic ether, *cis*,*cis*-2,2,6-trimethyl-3-oxabicyclo-[3.3.0]octane, *cis*,*cis*-**4** (6%, at 43% conversion; Table 1). Addition of biphenyl (**BP**) as cosensitizer did not affect the product distribution significantly. The analogous reaction in acetonitrile produced significantly lower yields of *cis*,*trans*-**3** (11%) and dramatically increased yields of three isomeric bicyclic ethers (**4**; 62% combined yield at 35% conversion; Table 1).



The irradiation of 1,4-dicyanobenzene (**DCB**) and (*E*)-**1** in methylene chloride resulted mainly in geometric isomerization to nerol (*Z*)-**1**, ∼60%), in addition to the formation of *cis*,*trans*-**3** (25%) and of three bicyclic ethers (**4**; 10% combined yield, at 39% conversion; Table 1). The corresponding irradiation of **DCB** and (*E*)-**1** in acetonitrile resulted in the formation of three isomeric bicyclic ethers (in 26% combined yield), and three stereoisomers of 6-(4-cyanophenyl)-2,2-dimethyl-3-oxabicyclo-[3.3.0]octane (**5**) (total yield, 46% at 70% conversion; Table 1). Addition of phenanthrene (**Ph**) as a cosensitizer increased the degree of isomerization and the total yield of the isomers of structure **5**.



Irradiation of **DCB** in the presence of phenanthrene (**Ph**) as cosensitizer and (*E*,*E*)-**2** in acetonitrile gave rise to three different

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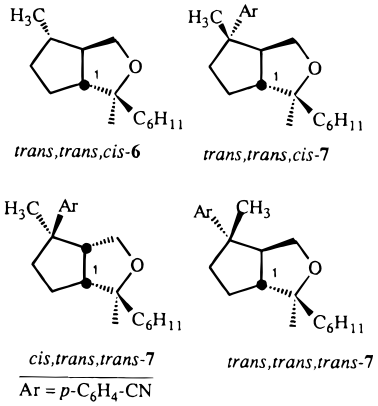
product types: 27% (*Z,E*)-**2** (geometric isomerization about the C2−C3 bond); 17% bicyclic ethers without an aryl substituent, mostly the *trans,trans,cis*-isomer (**6**; 11%); and bicyclic ethers containing a cyanomethyl group (type **7**), including 19% *trans,trans,cis*-**7**, 10% *cis,trans,trans*-**7**, and 8% *trans,trans,trans*-**7**. Because of the extensive *cis*−*trans* isomerization, the yields are given for 18 % conversion. The spectral features allowing the assignment of the key products are briefly discussed below.[10]



Discussion

These results establish several interesting facts concerning the reactivity of the radical cations (or their mechanistic equivalents): (1) electron transfer photo-oxidation of the hexa-1,5-dienes, **1** and **2**, in solution leads to five-center C−C cyclization; essentially all products isolated from these reactions are formed via this reaction type; (2) the primary cyclization product(s) may react by forming cyclopentane derivatives with an unsaturated side chain (**3**), apparently by hydrogen transfer from the isopropyl group to the five-membered ring; (3) alternatively, the primary cyclization product(s) undergo intramolecular nucleophilic capture, completing an unprecedented "tandem" cyclization (→**4** − **7**), via (a) bicyclic free radical(s); (4) the tandem cyclization products either have the same composition as the starting material (**4**, **6**) or contain a *p*-cyanophenyl moiety (**5**, **7**), indicative of an aromatic substitution; and (5) in competition with the formation of monocyclic or bicyclic products, (*E*)-**1** and (*E,E*)-**2** undergo (*E,Z*)-isomerization.

These findings pose several interesting questions about the key intermediates in these reactions, about the mechanism of the geometric isomerization, about the factors preventing or causing the second cyclization, and whether the method of oxidation or the medium influence the course of the reaction. The following discussion will focus on some of these issues.

The sensitized electron transfer photochemistry of many donor substrates proceeds via a series of simple steps (Scheme 1). The reaction is initiated by photoexcitation (eq 1) and involves electron (eq 2a) or charge transfer from the donor to the excited state acceptor (eq 2b). The radical cations are scavenged by methanol (eq 3), and the resulting methoxy substituted free radicals either form simple methanol adducts (e.g., by reduction−protonation, eq 4)[3a−c] or generate more complex products by aromatic substitution at the *ipso*-carbon of the sensitizer radical anion (eq 5).[3d−g] The detailed reaction sequence generating the three-component products is very well-established for olefins. This variant of the reaction is known as the photo-NOCAS reaction (for photo-induced nucleophile−olefin−combination aromatic substitution),[12b,c] and the three-component products are known as NOCAS products.

Scheme 1

Excitation

$$\mathbf{A} \longrightarrow {}^1\mathbf{A}^* \quad (1)$$

Electron/Charge Transfer

$$^1\mathbf{A}^* + \mathbf{D} \longrightarrow \mathbf{A}^{\bullet-} + \mathbf{D}^{\bullet+} \quad (2a)$$

$$^1\mathbf{A}^* + \mathbf{D} \longrightarrow \mathbf{A}^{\delta-} — \mathbf{D}^{\delta+} \quad (2b)$$

Nucleophilic Capture

$$\mathbf{D}^{\bullet+} + CH_3OH \longrightarrow \bullet[\mathbf{D}\text{–}OCH_3] + H^+ \quad (3)$$

Reduction-Protonation

$$\bullet[\mathbf{D}\text{–}OCH_3] + \mathbf{A}^{\bullet-} \longrightarrow [\mathbf{D}\text{–}OCH_3]^- + \mathbf{A} \quad (4a)$$

$$[\mathbf{D}\text{–}OCH_3]^- + H^+ \longrightarrow H\text{-}[\mathbf{D}\text{–}OCH_3]^- \quad (4b)$$

Aromatic Substitution

$$\bullet[\mathbf{D}\text{–}OCH_3] + \mathbf{A}^{\bullet-} \longrightarrow \mathbf{p}\text{-}CN\text{-}C_6H_4\text{–}\mathbf{D}\text{–}OCH_3 + CN^- \quad (5)$$

Scheme 2

Radical Cation Cyclization

$$\mathbf{D}^{\bullet+} \longrightarrow \mathbf{c}\text{-}\mathbf{D}^{\bullet+} \quad (6)$$

Intramolecular Nucleophilic Capture

$$\mathbf{c}\text{-}\mathbf{D}^{\bullet+} \longrightarrow \mathbf{bc}\text{-}\mathbf{D}^{\bullet} + H^+ \quad (7)$$

Reduction-Protonation

$$\mathbf{bc}\text{-}\mathbf{D}^{\bullet} + \mathbf{A}^{\bullet-} + H^+ \longrightarrow \mathbf{bc}\text{-}\mathbf{D}\text{-}\mathbf{H} + \mathbf{A} \quad (8)$$

Aromatic Substitution

$$\mathbf{bc}\text{-}\mathbf{D}^{\bullet} + \mathbf{A}^{\bullet-} \longrightarrow \mathbf{Ar}\text{–}\mathbf{bc}\text{-}\mathbf{D} + CN^- \quad (9)$$

The dienol radical cations, $\mathbf{1}^{\bullet+}$, $\mathbf{2}^{\bullet+}$, may also react intramolecularly, forming monocyclic bifunctional species (Scheme 2, eq 6), which may undergo intramolecular nucleophilic capture ("tandem cyclization"; eq 7). The resulting bicyclic free radicals may react with the sensitizer radical anion by reduction−protonation (eq 8) or aromatic substitution (eq 9).

Energetic Considerations. The energetics of individual steps provide a convenient preliminary measure for their feasibility. Thus, the reaction of excited singlet 1,4-dicyanobenzene (**DCB**) with **1** or **2** is unlikely to proceed by energy transfer, since the singlet excited state energy of **DCB**[11] is of the same order of magnitude as those of trisubstituted alkenes.[12] In contrast, electron transfer from the donor substrates to ^{1}**DCB*** (eq 2) should be efficient, regardless of the solvent.[13,14] A driving

(9) (a) For analogous reactions in sodium dodecyl sulfate micelles see: Hoffmann, U.; Gao, Y.; Pandey, B.; Klinge, S.; Warzecha, K.-D.; Krüger, C.; Roth, H. D.; Demuth, M. *J. Am. Chem. Soc*., **1993**, *115*, 10358−10359. (b) For analogous reactions in acetonitrile−water see: Warzecha, K.-D.; Xing, X.; Demuth, M.; Goddard, R.; Kessler, M.; Krüger, C. *Helv. Chim. Acta*, **1995**, *78*, 2065−2076.

(10) NMR spectral data for compounds **3**−**7** are available as Supporting Information. In the bicyclic compounds, **4**−**7**, the first stereochemical indicator designates the ring fusion; for **4** and **5**, the second indicator signifies the stereochemical relation at C6 relative to C1; for **6** and **7**, the second and third indicators signify the stereochemical relation at C2 and C6, respectively, relative to C1.

(11) $E_{0,0}$ = 4.3 eV: Arnold, D. R.; Maroulis, A. J. *J. Am. Chem. Soc.* **1976**, *98*, 5931.

(12) Flicker, W. M.; Mosher, O. A.; Kuppermamm, A. *Chem. Phys. Lett.* **1975**, *36*, 56.

(13) The free energies of radical ion pair formation were calculated according to a modified formulation of the Rehm−Weller equation accounting for different solvent polarities,[15] $-\Delta G^\circ_{SSIP} = E_{0,0} - E^\circ_{D^{\bullet+}/D} + E^\circ_{A/A^{\bullet-}} - [2.6\ \text{eV}/\epsilon - 0.13\ \text{eV}]$, where $E_{0,0}$, $E^\circ_{D^{\bullet+}/D}$, and $E^\circ_{A/A^{\bullet-}}$ are the values measured in acetonitrile, and 2.6 eV/ϵ − 0.13 eV is an empirical term introduced to correct for changes in solvent polarity.[15a]

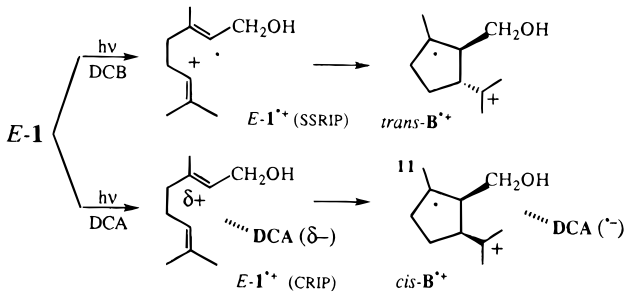
(14) The oxidation potentials of **1** and **2** are estimated as ∼2.0 V in analogy to limonene, ∼2.1 V,[3g] and methylcyclohexene, ∼1.93 V.[16] Given the reduction potential of **DCB** ($E_{A^-/A}$ = −1.60 V),[17] the oxidation of **1** or **2** by ^{1}**DCB*** (eq 2) in CH_3CN (ϵ = 37.5) and CH_2Cl_2 (ϵ = 9) are exergonic, $-\Delta G_{ET}$ = ∼0.8 and 0.5 eV, respectively.

force, $-\Delta G_{ET} \geq 0.5$ eV, is typically sufficient to generate solvent separated radical ion pairs (SSRIP). Accordingly, the photoreactions with **DCB** as sensitizer can be viewed as radical cation reactions.

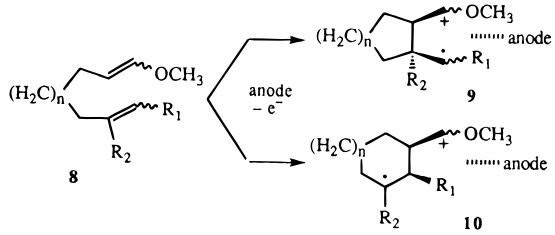
With 9,10-dicyanoanthracene (**DCA**) as sensitizer the low excited state energy of **DCA**[17,18] clearly rules out energy transfer to the diolefin substrates. On the other hand, electron transfer from **1** or **2** to ^{1}**DCA*** is modestly exergonic in CH_3CN, but slightly endergonic in CH_2Cl_2.[18] Donor acceptor pairs with marginal driving force for electron transfer typically form contact radical ion pairs (CRIP), in which the sensitizer radical anion serves as a complexing reagent, or template for an intramolecular reaction of the dienol radical cations. If different radical ion pairs are, indeed, involved in the photoreactions with different acceptor sensitizers, they may account for the unusually divergent electron transfer induced reactions of the 1,5-dienols.

1,5-Cyclization of 1,5-Diene Radical Cations. The electron transfer photosensitized 5-center C−C cyclization of 1,5-diene substrates is one of the significant findings of our study. This reaction yields one of two isomeric di-tertiary, 2,α-bifunctional methylidenecyclopentyl radical cations, *cis*- or *trans*-**B**$^{\bullet+}$ (or their mechanistic equivalents). All products isolated from these reactions are formed by this pathway, although the formation of (*Z*)-**1** and (*Z*,*E*)-**2** from **B**$^{\bullet+}$ may not be immediately obvious. The importance of this reaction type is well-known in photoreactions of nonconjugated dienes (rule of five)[7] and has also been established for nonconjugated alkenyl radicals.[8] The results reported here extend this reaction type to radical cations in homogeneous solution. Interestingly, the cyclization takes a different stereochemical course for the two sensitizer systems: the **DCA** sensitized reaction in CH_2Cl_2 predominantly yields the *cis*-fused intermediate (*cis*-**B**$^{\bullet+}$), whereas **DCB** induces cyclization mainly to the *trans*-fused intermediate (*trans*-**B**$^{\bullet+}$).

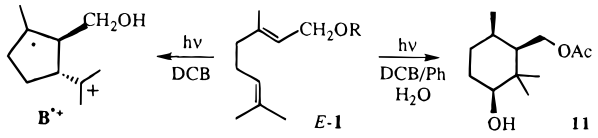
The divergent cyclizations are readily explained by the different primary intermediates inferred from the electron transfer energetics. The highly exothermic electron transfer to ^{1}**DCB*** favors the formation of solvent separated radical ion pairs (SSRIP) whereas the marginal driving force for electron transfer to ^{1}**DCA*** only permits the formation of contact radical ion pairs (CRIPs). Radical cations of SSRIPs are unencumbered by the counter ion and tend to form the (thermodynamically) more stable, *trans*-fused intermediate (*trans*-**B**$^{\bullet}$). In contrast, radical cations which are part of a CRIP cyclize in a fashion that does not interfere with the complexing partner, favoring *cis*-fused bifunctional intermediates (*cis*-**B**$^{\bullet}$). CRIPs have been invoked previously to explain the stereochemical course of electron transfer induced cycloaddition reactions.[19] Considering the shorter lifetimes of CRIPs (because of faster recombination), the products formed from CRIPs are considered "kinetic" products.



In this context, we mention the cyclizations of electron-rich 1,*x*-dienes (**8**; $n = 1-3$) upon anodic oxidation.[20,21] These reactions have been explained as reversible "radical-like" cyclizations;[21] their regiochemistry is determined apparently by the relative stability of the radical site in the cyclized radical cation and by its ease of oxidation. These reactions "occur at or near the electrode surface" [20c] and show a slight preference for *cis*-fused products,[20,21] similar to the **DCA** sensitized reactions. Photo-sensitized cyclizations differ from reactions at an anode in several respects: the choice of electron acceptor and solvent can direct the photoreaction to mono- or bicyclic products (vide infra), formed predominantly via *cis*- or *trans*-intermediates; in the photoreaction the (cyclized) radical cations are *reduced* by the sensitizer radical anion wheras, at the anode, they are *oxidized*.



Finally, the regiochemistry of the cyclization of **1** and **2** is affected if the photoreaction is carried out in the presence of water. For example, **1**, **2**, and their diterpene homolog, geranylgeraniol acetate, react exclusively by six-center cyclization (→**11**), when the photoreactions are carried out in sodium dodecyl sulfonate (SDS) micelles[9a] or in acetonitrile−water.[9b] Under these conditions, the radical cation is captured by water, and the resulting free radicals undergo 1,6-cyclization.



Competing Reactions of Monocyclic Bifunctional Radical Cations. The primary intermediates resulting from the reaction of (*E*)-**1** and (*E*,*E*)-**2** with ^{1}**DCA*** and ^{1}**DCB***, respectively, react to form different products. The bifunctional species generated with **DCA** (mainly *cis*-**B**$^{\bullet+}$), forms monocyclic products (**3**), whereas the intermediate generated with **DCB** (mainly *trans*-**B**$^{\bullet+}$) undergoes a second cyclization, forming bicyclic ethers (**4** or **5**).

In an attempt to rationalize the divergent course of the **DCA** and **DCB** sensitized reactions, we consider the competing reactions of the primary bifunctional radical cations, **B**$^{\bullet+}$. These

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(18) Given the reduction potential of **DCA** ($E_{A^-/A} = -0.9$ V),[17] and its low excited state energy ($E_{0,0} = 2.88$ eV),[17] the oxidation of **1** or **2** by ^{1}**DCA*** is mildly exergonic ($-\Delta G_{ET} \sim 0.1$ eV) in CH_3CN, but slightly endergonic ($-\Delta G_{ET} \sim -0.2$ eV) in CH_2Cl_2.

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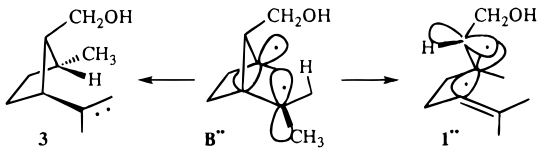
species may undergo back electron transfer (BET), H transfer (HTr), and intramolecular nucleophilic capture (INC), among other reactions. Since HTr and INC are intramolecular reactions, their rates should not be affected significantly by changes in the reaction conditions. In contrast, BET from the radical anion to $\mathbf{B}^{\bullet+}$ could depend critically on sensitizer and solvent. In fact, the key to the divergent results with the two sensitizer systems may lie in different BET rates. The predominant formation of bicyclic products in the **DCB** sensitized reaction suggests that INC is faster than the competing reactions, BET and HTr. On the other hand, the formation of monocyclic products in the **DCA** sensitized reaction suggests that INC is suppressed by a faster reaction, most likely BET.

The suggested different BET rates in the two sensitizer/solvent systems are compatible with the involvement of different types of radical ion pairs: the exothermic electron transfer to ^{1}**DCB*** favors SSRIPs whereas the marginal driving force for electron transfer to ^{1}**DCA*** causes the formation of CRIPs. The back electron transfer rates of CRIPs[22] and SSRIPs[23] follow an inverted free energy relationship. Accordingly, CRIPs are expected to have noticeably faster BET rates than SSRIPs, because their pair energies are lower.[24] Concerning the 2,α-bifunctional methylidenecyclopentyl radical cations $\mathbf{B}^{\bullet+}$, recombination in the SSRIP, $\mathbf{B}^{\bullet+}/\mathbf{DCB}^{\bullet-}$, in CH_3CN ($\epsilon = 37.5$) is more exergonic by ~0.5 eV than the corresponding reaction of the CRIP, $\mathbf{B}^{\bullet+}/\mathbf{DCA}^{\bullet-}$, in CH_2Cl_2 ($\epsilon = 9$). A free energy difference of this magnitude is expected to cause noticeably different BET rates. These considerations lead to the following order of rate constants:

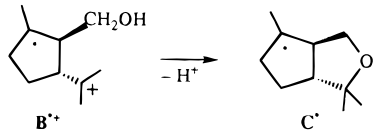
$$k_{et,c} \gg k_{inc} > k_{et,ss} > k_{htr}$$

Given the combination of rapid BET (forming $\mathbf{B}^{\bullet\bullet}$) and slow HTr in the radical cation, $\mathbf{B}^{\bullet+}$, products **3** must be formed via $\mathbf{B}^{\bullet\bullet}$. These 1,4-biradicals react by two competing reactions typical for biradicals. An intramolecular hydrogen migration would generate products of type **3**, whereas a fragmentation would generate a more localized biradical (e.g., $\mathbf{1}^{\bullet\bullet}$), cleaving the C−C bond formed earlier (by the radical cation) en route to the geometric isomer of the substrates (e.g., (*Z*)-**1**). In this mechanistic scheme, the significant yields of isomerized substrates formed upon **DCB** sensitization in less polar solvents (dichloromethane) is a necessary complement to the hydrogen transfer reaction. The intramolecular nature of the hydrogen transfer fully accounts for the observation that the 2-propenyl function is exclusively *trans* to the methyl group for all isomers of **3**.



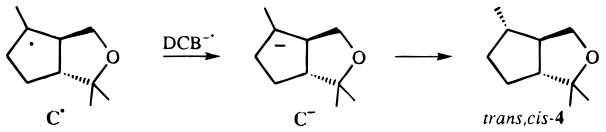
While the nature of the radical ion pairs dictates the stereochemistry of the bifunctional radical cations, $\mathbf{B}^{\bullet+}$, as well as the rate of BET, the stereochemistry of the cyclized radical cations does not appear to affect their reactivity dramatically. Thus, both *cis*- and *trans*-$\mathbf{B}^{\bullet+}$ undergo BET/intramolecular H transfer, leading to *cis*- and *trans*-**3**; likewise, both *cis*- and *trans*-$\mathbf{B}^{\bullet+}$ undergo intramolecular nucleophilic capture, leading to *cis*- and *trans*-fused products (e.g., *cis,trans*-**4** in addition to *trans, cis*-**4**).

Cyclization of 2,α-Methylidenecyclopentyl Radical Cations. The tandem cyclizations leading to **4** and **5** or **6** and **7** are without precedent in the chemistry of radical cations, although each step in itself is well documented. The formation of products **4**−**7** (R = H, C_6H_4-*p*-CN) is compatible with an intramolecular nucleophilic capture of the cationic site in the bifunctional radical cation ($\mathbf{B}^{\bullet+}$) with deprotonation.

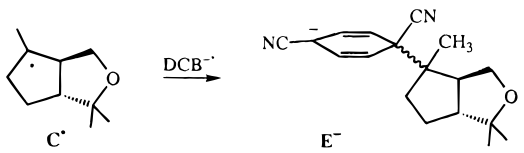


Intermolecular capture is very well established,[3a−c] but only a few cases of intramolecular capture have been documented. They include trapping alkene or diene radical cations by a carboxylic acid moiety[25] or an alcohol function,[26] and capture of a 1,3-cyclopentanediyl radical cation by an alcohol function tethered to the bridgehead,[27] and the intramolecular reaction of chrysanthemol.[28]

The bicyclic free radical, $\mathbf{C}^{\bullet}$, resulting from the tandem cyclization, reacts with the sensitizer radical ion to generate the products. The formation of product **4** most likely occurs via electron transfer from the sensitizer radical anion and subsequent protonation of the anion. The predominant formation of *trans,cis*-**4** is explained as a protonation on the face of the intermediate opposite to the *gem*-dimethyl function; this can be ascribed to steric reasons.



The formation of the isomeric products **5** amounts to an aromatic substitution by $\mathbf{C}^{\bullet}$ on the sensitizer radical anion. This reaction sequence is reminiscent of the photo-induced nucleophile−olefin−combination aromatic substitution reaction (photo-NOCAS).[3d−g] The aromatic substitution reported here is preceded by a tandem cyclization, including an intramolecular nucleophilic capture (hence, tandem cyclization−intramolecular nucleophilic capture−aromatic substitution, TC-INCAS). The formation of **5** (R = C_6H_4-*p*-CN), requires coupling between $\mathbf{C}^{\bullet}$ and the sensitizer radical anion. These reactions would yield an adduct anion, $\mathbf{E}^-$, which is stabilized by loss of cyanide ion ($\mathbf{C}^{\bullet} \rightarrow \mathbf{E}^- \rightarrow \mathbf{5} + CN^-$).



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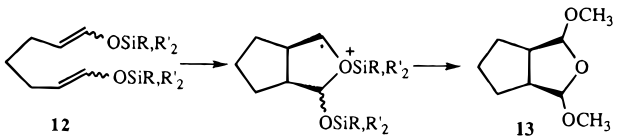
Reactions resembling the tandem cyclizations reported here have been noted also during anodic oxidation.[20b,c] For example, the bis(*tert*-butyldimethylsiloxy enol ether), **12**, in the presence of methanol was converted to 2,4-dimethoxy-3-oxabicyclo[3.3.0]-octane.[20c] The formation of **13** requires a complex reaction sequence, including two separate oxidation steps, the release of two silyl cations, and the incorporation of two methoxy groups.



Conclusion

In summary, we report two examples of an unprecedented electron transfer induced tandem cyclization. The course of the reaction is governed by the free energy of electron transfer. Systems with marginal driving force give rise to CRIPs, resulting in *cis*-fused, monocyclic products; systems permitting exergonic electron transfer form SSRIPs and generate *trans*-fused, bicyclic products. These findings expand the scope of radical cation reactivity. In contrast to other substrates known to undergo electron transfer sensitized C−C cyclizations, the molecules discussed here contain only methyl groups as activating and directing functions. Our results suggest a wide range of substrates which may undergo analogous reactions. Studies to explore the limitations of this reaction are currently under investigation.

Experimental Section

Materials and Solvents. Geraniol (Aldrich; 98%) and (*E*,*E*)-farnesol (Aldrich; 96%) were used as received. Phenanthrene (**Ph**; Aldrich; 98%), 9,10-dicyanoanthracene (**DCA**; Eastman Kodak), and 1,4-dicyanobenzene (**DCB**; Aldrich; 98%) were purified by recrystallization. Acetonitrile (Fischer) and methylene chloride (Fischer) were distilled from calcium hydride and stored over 4A molecular sieves in brown bottles under argon atmosphere.

Exploratory Photoreactions. Solutions (1-mL) containing 0.1 M donor, 0.03−0.1 M sensitizer, and 0.01 *g* of *n*-$C_{12}H_{26}$ (added as GC internal standard) in various solvents with or without cosensitizer were purged with argon for 15 min and irradiated in a Rayonet RPR-100 photoreactor equipped with 16 lamps. For reaction mixtures containing **DCA** or **DCB**/**Ph** RPR-3500 lamps were used, whereas for those containing **DCB** as sole sensitizer RPR-3000 lamps were employed. The progress of the reaction was monitored by gas chromatography on a GC/MS system (HP 5890 series II GC interfaced with an HP 5971 mass selective detector), using a 12 m × 0.2 mm × 0.33 μm HP-1 capillary column (cross-linked methyl silicone on fused silica). The major products are summarized in Table 1.

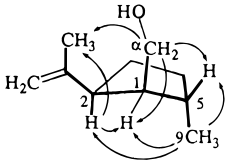
Isolation of Products. Reaction products were isolated by liquid column chromatography and, in some cases, further purified by preparative GC. Reaction products formed in yields >∼4% were isolated by a series of column chromatographic procedures on a set of 50-cm columns with IDs ranging from 1 to 5 cm, packed with ∼15 cm of TLC standard grade silica gel (Aldrich; without binder) and eluted with solvent gradients, usually from light petroleum ether (bp < 65 °C) to mixtures with either methylene chloride or ethyl acetate. Typically, several passes were required to isolate the products. Preparative GC was carried out on a 6-ft column packed with 10% CP-5 on a Chromosorb WHP support.

Preparative Photoreaction of Geraniol with DCA in CH_2Cl_2. A sample containing 1.54 g of geraniol (0.1 M), 0.45 g of **DCA** (saturated, ∼0.02 M) in 100 mL of CH_2Cl_2 was irradiated in a 30-mm ID Pyrex tube for 100 h to ∼30% conversion of geraniol. The reaction mixture was concentrated to ∼5 mL, 3 g of silica gel added, and the resulting slurry evaporated to dryness. The residue was loaded onto a silica gel column and eluted with petroleum ether−ethyl acetate, gradually changing from pure petroleum ether to mixtures containing up to 20% v/v ethyl acetate. The products are eluted in the order: *cis*,*cis*-**4**, *cis*,*trans*-**3**, *trans*,*cis*-**3**, and geraniol. The fractions containing the individual compounds were combined, concentrated, and further purified by preparative GC for NMR analysis. The major product, *cis*,*trans*-**3**, was obtained as a ∼0.5 mL sample containing solvent as only impurities; purification by GC gave ∼100 mg (∼20% yield) of pure material.

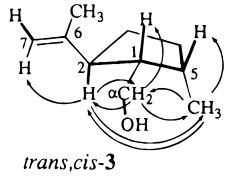
Preparative Photoreaction of Geraniol with DCA in CH_3CN. A sample containing 1.54 g of geraniol (0.1 M), 0.23 g of **DCA** (saturated, ∼0.01 M) in 100 mL of CH_3CN was irradiated in a 30-mm ID Pyrex tube for 10 days to ∼40% conversion of geraniol. The reaction mixture was worked up and chromatographed as described above. The isomers of **4** were eluted before **DCA** and geraniol; removal of solvent gave 0.3 g (∼50% yield) of an oily residue, containing *trans*,*cis*-**4** (∼45%), *trans*,*trans*-**4** (∼20%), and *cis*,*trans*-**4** (∼35%). Purification of this mixture by preparative GC gave 0.1 g (∼15% yield) of pure *trans*,*cis*-**4**, and a mixture of *trans*,*trans*-**4** and *cis*,*trans*-**4**.

Characterization of Products. Structure assignments of isolated products rest on MS and NMR data, including the results of DEPT, two-dimensional COSY, and HETCOR experiments, where appropriate. Extensive NOE difference spectra were taken to elucidate substituent stereochemistry and spatial relation between different groups, and to confirm the structure. Proton NMR spectra were recorded on either a Varian XL-400 or a Varian VXR-200 spectrometer. ^{13}C and HETCOR spectra were recorded on the Varian VXR-200 spectrometer operating at 50.3 MHz.

Structure Identification. The stereochemistry of *cis*,*trans*-**3** rests on NOE evidence. Irradiating either of the hydroxymethyl resonances caused NOE enhancement of the allylic methyl signal, but not the (allylic) H_2 signal: the hydroxymethyl must be *cis* to the isopropenyl group. Irradiation of the non-allylic methyl signal (attached to C_5) leads to enhancement of H_2, placing the methyl group (at C_5) *trans* to isopropenyl and hydroxymethyl groups.

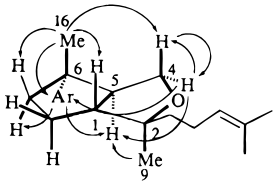


cis,*trans*-**3**

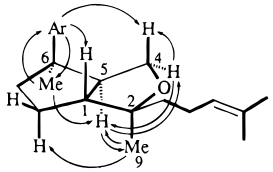


trans,*cis*-**3**

The major isomer of **7** is identified by a series of NOE experiments. Irradiation of the methyl (C_{16}, attached to C_6) caused enhancements for the H_1 and H_{4ax} signals, but not for H_5, indicating a *trans*-fused ring system with the aryl group *cis* to C_2. Irradiation of the *o*-aryl resonance confirmed the orientation of the aryl group by enhancement of the adjacent methyl (C_{16}) and H_5. Finally, irradiation of the methyl group (C_9) attached to C_2 resulted in enhancement of the H_5 signal; the proximity of these groups shows the *trans*-orientation of the 4-methyl-3-pentenyl residue. The major isomer is *trans*,*trans*,*cis*-**7**.



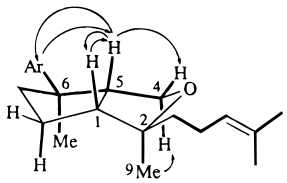
trans,*trans*,*cis*-**7**



trans,*trans*,*trans*-**7**

The stereochemistry of *trans*,*trans*,*trans*-**7** is based on three NOE experiments. Irradiating the *o*-aryl frequency enhances the signals of H_1 and H_{4ax}, but not H_5: the ring is *trans*-fused; irradiating the methyl (C_{16}) resonance enhances the *o*-aryl and H_5 signals: the aryl lies *trans* to C_2; lastly, irradiation of the methyl (C_9) attached to C_2 caused enhances the H_5 resonance, establishing the *trans*-orientation of the 4-methyl-3-pentenyl residue.

The *cis,trans,trans*-isomer is *cis*-fused because of the strong mutual NOE response between H_1 and H_5. Irradiation of H_5 also enhances the *o*-aryl signal and the (strongly deshielded) H_{4x}; thus, the aryl occupies the exo position, *cis* to H_5. The stereochemistry at C_2 is shown by the enhancement of H_{4n} upon irradiating the methyl signal, C_9, attached to C_2.



cis,trans,trans-**7**

Significant NOE interactions between the aryl functions of **7** and the γ-protons at C_4 demonstrate the proximity of these functions. One isomer, *trans,trans,trans*-**7**, has a strongly shielded signal (H_{4ax});[11] thus, H_{4ax} lies in the shielding cone of the aryl group. The aryl functions of *trans,trans,cis*- and *cis,trans,trans*-**7** cause no significant magnetic shielding.

Having established the stereochemistry of three isomers of **7**, the stereochemistry of the remaining structure types is based on a comparison between the vicinal (^3J) and geminal (^2J) $^1H-^1H$ coupling constants and the chemical shifts of the four structure types, **4**−**7** (see Table 2 in the Supporting Information). The axial H_{4ax} of *trans,trans*-**5** and *trans,trans,trans*-**7**, are strongly shielded, reflecting their location in the shielding cone of the aryl ring.[29] In general, *trans*-fused isomers have large vicinal coupling ($^3J_{1-5} \approx 13-14$ Hz), in keeping with general trends.[30]

The stereochemistry at C_6 of the ethers, **4** and **6**, is based on a shielding anisotropy argument. The equatorial protons of cyclohexanes are deshielded by ~0.5 ppm compared to the axial protons;[31] this fact is widely applied in structural elucidation.[32] Analogously, the proton H_6 of the bicyclic ethers should be deshielded by the C_1-C_5 and C_7-C_8 bonds, if it occupies the equatorial position. The *trans*-fused ring system is rigidly held in a conformation where the group opposite to H_5 occupies a pseudo-axial position. Accordingly, products with lower chemical shifts for H_6 (~1.7 ppm) are assigned structures with an axial H_6, viz., *trans,trans,cis*-**6** and *trans,cis*-**4**. Conversely, products with higher chemical shifts for H_6 (~2.1 ppm) are assigned structures with axial CH_3, i.e., *trans,trans,trans*-**6** and *trans,trans*-**4**.

Acknowledgment. Financial support of this work by the National Science Foundation through Grants NSF CHE-9110487 and CHE-9414271 and an equipment grant, NSF CHE-9107839, is gratefully acknowledged. The work of C.S. was supported by an NSF undergraduate equipment grant, NSF USE-9250530, for the purchase of a 200-MHz FT NMR spectrometer.

Supporting Information Available: NMR spectral assignments for products **3**−**7** (16 pages). See any current masthead page for ordering and Internet access instructions.

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