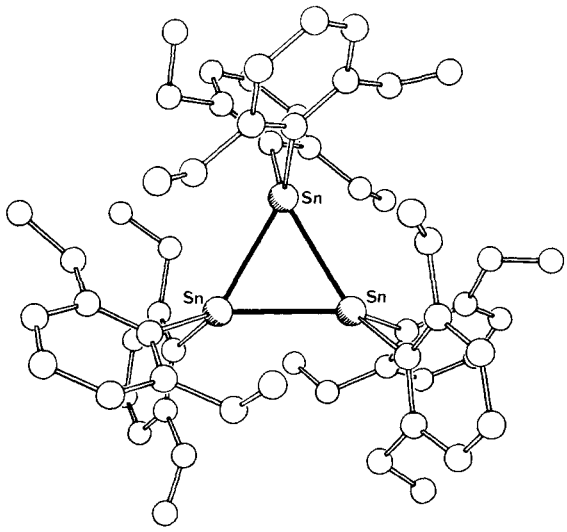

Figure 2. Crystal structure of **2**: Sn–Sn bond lengths 2.870 (1), 2.856 (1), and 2.854 (1) Å; Sn–Sn–Sn bond angles 59.8 (1), 59.9 (1), and 60.3 (1)°; C–Sn bond lengths 2.167 (10)–2.203 (9) Å.

coloration. The usual workup, including flash chromatography (5:1 petroleum ether/benzene), provides after recrystallization from benzene orange crystals, mp 175 °C with decomposition, in 53% yield, that exhibit physical properties fully consistent with the trimeric structure $(C_{20}H_{26}Sn)_3$: mass spectrum (field desorption) $M^{+\cdot}$ cluster m/z (1146–1164);[7] ^{119}Sn NMR (benzene) δ (ppm from Me_4Sn) −416.52. Resembling distannanes[9] and the silicon analogue,[4] compound **2** shows an ultraviolet absorption maximum at 295 nm (log ϵ 4.66, cyclohexane), and due to the expected slow rotation of the aryl rings along the tin and carbon bonds, the ^1H NMR spectra (250 MHz, toluene-d_8) of the ethyl groups are temperature dependent.[4] Thus, two triplets (δ 0.89 and 0.69) and a complex multiplet (centered at 2.83 ppm) observed at −20 °C collapse to one triplet (δ 0.77) and one quartet (δ 2.78) at 60 °C, respectively. Confirmation of the structures assigned above to **1** and **2** follows.

Crystallographic Analysis of 1. The crystal structure of **1** is shown in Figure 1.[10] The cyclotristannoxane ring is essentially planar with a maximum deviation from the least-squares plane of 0.02 Å[2b] and thus follows the trend of $(Ph_2MO)_3$ (M = Si, Ge) rings, which possess small torsional angles.[11] The Sn–O and Sn–Ar bond lengths are in the range of 1.929 (6)–1.961 (6)[12] and 2.138 (6)–2.169 (9) Å, respectively. The wide Sn–O–Sn angles of 135.6 (3), 135.9 (3), and 137.1 (3)° are characteristic for M–O–M (M = Si, Ge, Sn).[13] As outlined by Glidewell,[14] they can easily be attributed to nonbonded interactions rather than $p\pi$–$d\pi$ bonding.[15]

Crystallographic Analysis of 2. As shown in Figure 2,[16] the three tin atoms of **2** form an isosceles triangle, as in the trisilicon analogue[4] with Sn–Sn bond lengths of 2.870 (1), 2.856 (1), and 2.854 (1) Å, respectively. The angles at the tin atoms are 59.8 (1), 59.9 (1), and 60.3 (1)°, respectively. The planes formed by each of the pairs of Sn–Ar bonds are all rotated in the same sense by between 7.9 and 8.8° from the normal to the plane of the three tin atoms. The Sn–Ar bonds are in the range of 2.167 (10)–2.203 (9) Å. The Sn–Sn bond lengths of **2** appear to be the longest ever found for a bond of this type.[17] The slow rotation of the phenyl rings along the C–Sn bonds shown above by ^1H NMR spectra is expected from the steric congestion created between several pairs of the ethyl groups.

Compound **2** in the crystalline form is air-stable but is converted to **1** upon standing in solution. **2** is also reactive toward chlorinated solvents. Of particular interest is obviously its thermal and photochemical behavior, which will be discussed in due course.

Acknowledgment. We thank the National Science Foundation and Yoshitomi Pharmaceutical Industries, Ltd., Japan, for financial support. High-resolution mass spectra were provided by the facility supported by the National Institutes of Health (Grant RR 00317; principal investigator, Professor K. Biemann), from the Biotechnology Resources Branch, Division of Research Resoucres.

Registry No. 1, 84143-91-9; **2**, 84143-92-0; **3**, 16919-46-3; **4**, 84143-93-1.

Supplementary Material Available: Listing of atom coordinates and temperature factors, bond lengths, bond angles, and anisotropic temperature factors as well as detailed information concerning the mass spectra, X-ray analyses, and other spectral data (15 pages). Ordering information is given on any current masthead page.

(9) Drenth, W.; Janssen, M. J.; Van Der Kerk, G. J. M.; Vliegenthart, J. A. *J. Organomet. Chem.* **1964**, *2*, 265.

(10) Crystals of **1** solvated with benzene $C_{60}H_{78}Sn_3O_3 \sim {}^1/_2C_6H_6$ are monoclinic with a = 21.219 (3) Å, b = 13.246 (2) Å, c = 21.372 (3) Å, β = 97.21 (1)°, U = 5959 Å^3, space group $P2/c$, Z = 4, μ(Cu Kα) = 105 cm^{-1}. Three-dimensional intensity data were collected on a Nicolet R3m diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares calculations to R = 0.054 for 5263 observed reflections with $|F_o| > 3\sigma(|F_o|)$.[7]

(11) For $(Ph_2SiO)_3$: (a) Bokii, N. G.; Zakharova, G. N.; Struchkov, Yu. T. *J. Struct. Chem.* **1972**, *13*, 267. For $(Ph_2Ge\ O)_3$: (b) Ross, L.; Dräger, M. *Chem. Ber.* **1982**, *115*, 616.

(12) The Sn–O bond lengths are 1.955 Å in $(Ph_3Sn)_2O$ [(a) Glidewell, C.; Liles, D. C. *Acta Crystallogr., Sect. B* **1978**, *B34*, 1693] and 1.940 Å in $(Me_3Sn)_2O$ [(b) Vilkov, L. V.; Tarasenko, N. A. *Zh. Strukt. Khim.* **1969**, *10*, 1102].

(13) For $(Ph_2SiO)_3$: Si–O–Si angle of 130–133°, ref 11a. For $(Ph_2Ge\ O)_3$: Ge–O–Ge angle of 128–130°, ref 11b. For $(Ph_3Sn)_2O$: Sn–O–Sn angle of 137°, ref 12a.

(14) Glidewell, C. *Inorg. Chim. Acta* **1975**, *12*, 219.

(15) Replacement of oxygen by less electronegative sulfur reverts bond angles to the expected values rather than over more pronounced, i.e., $(Ph_2SnS)_3$, Sn–S–Sn angle of 104°: Schumann, H. *Z. Anorg. Allg. Chem.* **1967**, *354*, 192.

(16) Compound **2** solvated with benzene $(C_{60}H_{78}Sn_3 \cdot {}^1/_2\ C_6H_6)$ crystallized in the monoclinic system, space group $P2/c$, with a = 20.920 (7) Å, b = 13.086 (4) Å, c = 21.155 (5) Å, β = 97.12 (2)°, U = 5747 Å^3, Z = 4, μ(Cu Kα) = 108 cm^{-1}. The structure was solved in the same manner as for **1**; R = 0.057 for 5216 observed reflections with $|F_o| > 3\sigma(|F_o|)$.[7]

(17) The Sn–Sn bond lengths are 2.78 Å in $(Ph_2Sn)_6$ [(a) Olson, D. H.; Rundle, R. E. *Inorg. Chem.* **1963**, *2*, 1310], 2.839 Å in $[(Me_3SiCH_2)_2Sn]_4$ [(b) Belsky, V. K.; Zemlyansky, N. N.; Kolosova, N. D.; Borisova, I. V. *J. Organomet. Chem.* **1981**, *215* 41], and 2.77 Å in Ph_6Sn_2 [(c) Preut, H.; Haupt, H. J.; Huber, F. *Z. Anorg. Allg. Chem.* **1973**, *396*, 81].

Isoquinolinium Cycloadditions: Total Synthesis of (±)-14-Epicorynoline and *O*-Methylarnottianamide

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Bradsher[1] and others[2] have established that polar cycloaddition of isoquinoline salts with electron-rich alkenes is virtually 100% regiospecific and, for easily polarizable, unsymmetrical alkenes, highly stereospecific. The overall process disrupts the aza aromatic ring, creating a tricyclic system with up to four new stereocenters and an immonium ion.[3] We have investigated the general use

(1) (a) Chen, T.-K.; Bradsher, C. K. *J. Org. Chem.* **1979**, *44*, 4680–4683. (b) Day, F. H.; Bradsher, C. K.; Chen, T.-K. *Ibid.* **1975**, *40*, 1195–1198. (c) Bradsher, C. K. *Adv. Heterocycl. Chem.* **1974**, *16*, 289–324.

(2) Intramolecular version: Gisby, G. P.; Sammes, P. G.; Watt, R. A. *J. Chem. Soc., Perkin Trans. 1* **1982**, 249–255.

(3) In this study, a fifth stereocenter is created by subsequent addition of a nucleophile to the immonium ion. Under these conditions we assume the addition leads to the kinetic product, although the stereochemistry at this center does not alter the overall synthesis (see ref 2).

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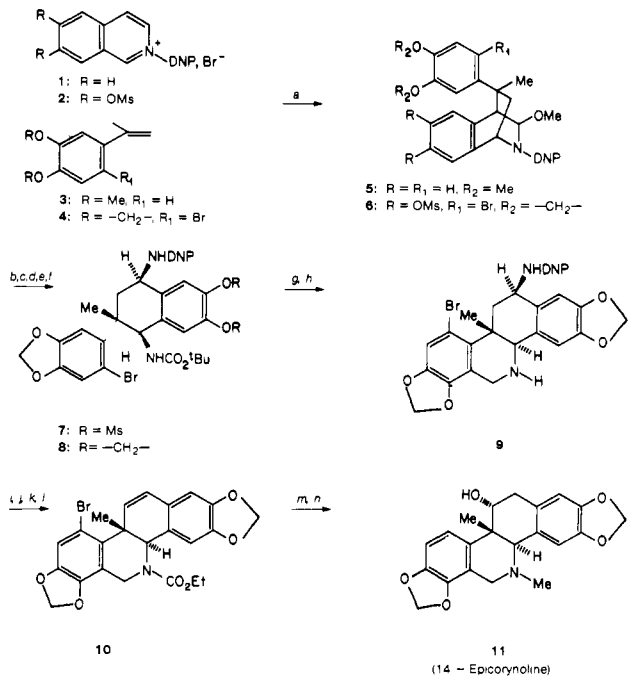
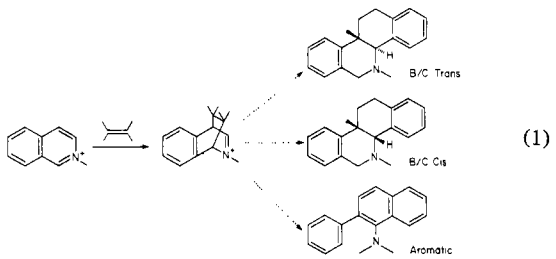
Scheme I



[a] $CaCO_3$, $MeOH/CH_2Cl_2$, 40 °C. [b] Amberlyst 15, THF/H_2O, (10:1), 40 °C, 16 h. [c] CrO_3, H_2SO_4, CH_3COCH_3, 0 °C, 30 min. [d] $(PhO)_2PON_3$, Et_3N, *t*-BuOH, reflux, 18 h. [e] 2 N NaOH/MeOH (1:1), 40 °C, 16 h. [f] $(ICH_2)Me_3N^+I^-$, Na_2CO_3, DMF, 50 °C, 12 h. [g] THF/H_2O/concentrated HCl (6:3:1), reflux, 4 h. [h] THF/MeOH/37% Formalin (2:2:1), reflux, 40 min; 16% HCl, room temperature, 16 h. [i] $ClCO_2Et$, Et_3N, CH_3COCH_3, 12 h. [j] IRA-400 (OH^-), CH_3COCH_3/H_2O (5:1), 20 h. [k] MeI, K_2CO_3, MeOH, 20 h. [l] IRA-400 (OH^-), MeOH, 40–50 °C, 20 min. [m] *m*-$ClC_6H_4CO_3H$, CH_2Cl_2, 10% $NaHCO_3$, 0 °C, 20 h. [n] LAH, THF, reflux, 3.5 h.

of this intriguing reaction in the context of a comprehensive approach to benzophenanthridine and biogenetically related alkaloids[4] (eq 1). Central to these studies were procedures to

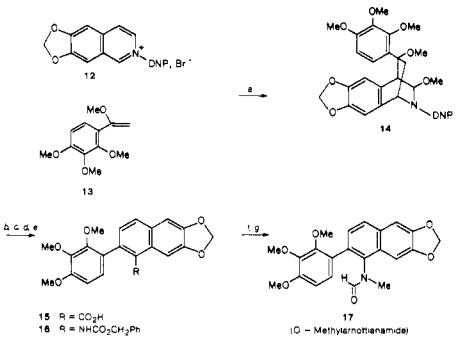


(1)

overcome some prior synthetic limitations,[1b,c] particularly as they effect unreactive or 3-unsubstituted isoquinolines. The results are illustrated herein by the total synthesis of (±)-14-epicorynoline (**11**) and *O*-methylarnottianamide (**17**).

We focused initially on the more elusive,[4] angularly methylated trans-fused benzophenanthridine series.[5] Our approach, outlined in Scheme I, predetermined the stereochemistry of the crucial B/C ring junction at an early stage by a highly regio- and stereospecific union of α-methylstyrenes with 2,4-dinitrophenyl (DNP) isoquinoline salts, e.g., treatment of **1**[6] in methanol/dichloromethane with 1.5 equiv of **3** in the presence of powdered calcium carbonate for 3 days quantitatively generated isomerically pure **5**. Other

Scheme II



[a] $CaCO_3$, MeOH, 40 °C, 30 h syringe drive, stir 10 h. [b] Amberlyst 15, THF/H_2O (10:1), 37 °C, 16 h. [c] 2.5 M NaOH/MeOH (1:2.5), reflux, 5 min. [d] CrO_3, H_2SO_4, CH_3COCH_3, 0 °C, 6 h. [e] $(PhO)_2PON_3$, Et_3N, $PhCH_2OH$, $PhCH_3$, reflux, 15 h. [f] $LiAlH_4$, THF, reflux, 8 h. [g] CCl_3CHO, $CHCl_3$, 0 °C → room temperature, 4 h, then reflux 2 h.

commonly used acid scavengers, inter alia, tertiary amines, glycidol, alumina, sodium bicarbonate, and acetate, were either ineffective in preventing dienophile polymerization or incompatible with **1** under the reaction conditions.

In extending this reaction to 14-epicorynoline (**11**), we could in no instance effect cycloaddition between styrene **4** and isoquinoline salts bearing strong electron-donating groups at C-6. This may in part reflect the pronounced inverse-electron-demand character[7] of isoquinolinium cycloadditions. However, the desired substitution pattern was accommodated by dimesylate **2**,[8] which underwent smooth cycloaddition at 40 °C yielding **6** (70–75%) and a small amount of free isoquinoline resulting from solvolysis.

Adduct **6** could be transformed without purification of intermediates into urethane **7** (72%) by hydrolytic cleavage, Jones oxidation, and diphenylphosphoryl azide[9] (DPPA) mediated Curtius rearrangement in *tert*-butyl alcohol. Selective mesylate saponification[10] and catechol bis-alkylation using (iodomethyl)-trimethylammonium iodide[11]/sodium carbonate in dimethylformamide evolved **8** (45%). Acidic hydrolysis of the *tert*-butyl urethane in **8** followed by Pictet–Spengler cyclization[12] using excess Formalin generated the B/C trans-fused benzophenanthridine **9**. Ethyl chloroformate derivatization introduced a latent *N*-methyl group and protected the annular nitrogen during selective dinitrophenyl hydrolysis *in acetone*,[13] exhaustive methylation, and Hofmann elimination,[14] yielding styrene **10** (33% overall from **8**). Epoxidation with buffered *m*-chloroperbenzoic acid from the less-hindered face and lithium aluminum hydride ($LiAlH_4$) reduction yielded (±)-14-epicorynoline (**11**, 54%) spectrally and chromatographically identical with an authentic sample.

Another facet of the basic theme is revealed (Scheme II) in the preparation of *O*-methylarnottianamide (**17**), representative of several alkaloids[15] biogenetically related to and readily interconvertible[16] with the aromatic benzophenanthridines. Slow

(4) For this paper we have adopted the benzophenanthridine numbering system used in ref 4a. Reviews: (a) Shamma, M.; Moniot, J. L. "Isoquinoline Alkaloids Research 1972–1977"; Plenum Press: New York, 1978. (b) Hearn, M. J.; Swanson, S. L. *J. Heterocycl. Chem.* **1981**, *18*, 207–222. (c) Phillips, S. D.; Castle, R. N. *Ibid.* **1981**, *18*, 223–232.

(5) Angularly methylated trans-fused benzophenanthridines may be the thermodynamically less stable arrangement (see ref 4a, pp 280–281).

(6) All compounds were fully characterized by spectral means and had satisfactory combustion analysis or high-resolution mass spectroscopy.

(7) Bradsher, C. K.; Walls, T. G.; Westerman, I. J.; Porter, N. A. *J. Am. Chem. Soc.* **1977**, *99*, 2588. See also ref 1.

(8) For a general isoquinoline synthesis see: Falck, J. R.; Manna, S.; Mioskowski, C. *J. Org. Chem.* **1981**, *46*, 3742–3745. Also: Birch, A. J.; Jackson, A. H.; Shannon, P. V. R.; Varma, P. S. P. *Tetrahedron Lett.* **1972**, 4789–4792.

(9) Shioiri, T.; Ninomiya, K.; Yamada, S.-I. *J. Am. Chem. Soc.* **1972**, *94*, 6203–6205. Ninomiya, K.; Shioiri, T.; Yamada, S.-I. *Tetrahedron* **1974**, 2151–2157.

(10) Bordwell, F. G.; Boutan, P. J. *J. Am. Chem. Soc.* **1957**, *79*, 717–722.

(11) Schreiber, J.; Maag, H.; Hashimoto, N.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 330–331.

(12) Brossi, A.; Schenker, F.; Schmidt, R.; Banziger, R.; Leimgruber, W. *Helv. Chim. Acta* **1966**, *49*, 403.

(13) Lloyd, P. F.; Stacey, M. *Tetrahedron* **1960**, 116–124.

(14) Kaiser, C.; Weinstock, J. *Org. Synth.* **1976**, *55*, 3–7.

(15) Ishii, H.; Ishikawa, T.; Lu, S.-T.; Chen, I.-S. *Tetrahedron Lett.* **1976**, 1203–1206. Ishii, H.; Ishikawa, T. *Heterocycles* **1976**, *5*, 275.

(16) Ishii, H.; Ishikawa, T.; Ichikawa, Y.-I.; Sakamoto, M. *Chem. Pharm. Bull.* **1977**, *25*, 3120–3121. Ishii, H.; Ishikawa, T. *Yakugaku Zasshi* **1981**, *101*, 663–687.

addition of the reactive α-methoxystyrene **13**[17] (2.5 equiv) by syringe drive over 30 h to a methanolic solution of DNP salt **12** at 40 °C and stirring for a further 10 h gave cycloadduct **14** (90%). The adduct was hydrolyzed by acid and then immediately aromatized[18] with strong alkali and the resultant aldehyde oxidized to naphthoic acid **15** (82% from **14**) by Jones reagent. DPPA rearrangement of **15** in dry toluene with added benzyl alcohol[9] afforded benzyl urethane **16**, which was reduced by $LiAlH_4$ and formylated with chloral[19] to give **17** indistinguishable from authentic material (36% overall from **15**).

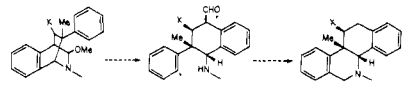
The foregoing examples help to define the scope of isoquinolinium cycloadditions and validate their potential in natural products synthesis. Further studies leading to cis-fused benzophenanthridines[20] and other classes of natural products are in progress.

Acknowledgment. This work was supported financially by the Robert A. Welch Foundation and NATO (RG 158.80). We are grateful to Professor Narao Takao for a sample of (+)-14-epicorynoline and Professor Hisashi Ishii for a sample of *O*-methylarnottianamide and his advice on its characterization and chemical behavior.

Registry No. 2, 84133-48-2; **4**, 84133-49-3; (±)-**6**, 84133-41-5; (±)-**7**, 84133-42-6; (±)-**8**, 84173-74-0; (±)-**9**, 84173-67-1; (±)-**10**, 84133-46-0; (±)-**11**, 83607-67-4; **12**, 83379-65-1; **13**, 84133-47-1; (±)-**14**, 84133-43-7; **15**, 84133-44-8; **16**, 84133-45-9; **17**, 84143-15-7.

Supplementary Material Available: Physical data for **2–7**, **9**, **10**, **13–15**, and **17** (2 pages). Ordering information is given on any current masthead page.

(17) Obtained as a colorless oil from 2,3,4-trimethoxyacetophenone by the following method: Loudon, G. M.; Smith, C. K.; Zimmerman, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 465.
(18) Manna, S.; Falck, J. R.; Mioskowski, C. *J. Org. Chem.* **1982**, *47*, 5021.
(19) Blicke, F. F.; Lu, C.-J. *J. Am. Chem. Soc.* **1952**, *74*, 3933–3934.
(20) Reversal of the regiospecificity observed with α-substituted styrenes offers, in principle, an expeditious route to cis-fused benzophenanthridines by incorporating the original isoquinoline nitrogen into ring C (eq i).



(i)

Cation Radical Catalyzed Olefin Cyclodimerization

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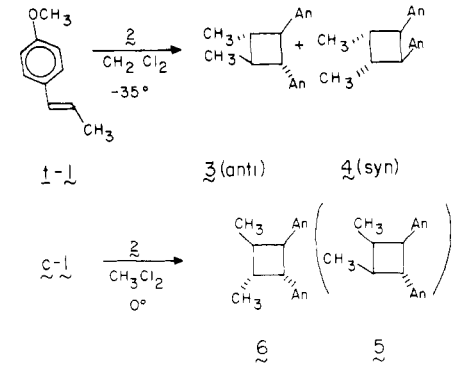
Received July 21, 1982

The cyclodimerization of *N*-vinylcarbazole giving *trans*-1,2-bis(*N*-carbazolyl)cyclobutane via a cation radical chain reaction, observed by Ledwith in 1969, in potentially one of the pioneering observations in cation radical pericyclic chemistry.[1] The mechanistic details of the cation radical cycloaddition step have not yet been clarified, but Ledwith and others have apparently assumed it occurs in stepwise fashion.[2,3] The fundamental interest in this question is enhanced by the recent observation of an apparently concerted path for the cation radical catalyzed Diels–Alder reaction.[4] A stereochemical study of the cation radical catalyzed dimerizations of *cis*- and *trans*-anethole (**1**, Scheme I) has now been carried out, which established these dimerizations as stereospecific. An MNDO theoretical reaction path study of the prototype cycloaddition of ethene cation radical and ethene, assisted by STO-3G ab initio calculations on the key intermediate, suggests a novel mechanism for such cycloadditions that is in full accord with the experimental determination of stereospecificity. Further, a synthetically attractive new procedure for olefin cyclodimerization, involving catalysis by tris(*p*-bromophenyl)-aminium hexachloroantimonate (**2**) in methylene chloride solution, is developed. The first cation radical cycloadditions of nonequivalent olefinic components are also reported.

Scheme I



The dimerization of *trans*- and *cis*-anethole (**1**) illustrates the new synthetic procedure and also illuminates the reaction stereochemistry. When added to a methylene chloride solution containing 5 mol% of **2** at 0 °C, *trans*-**1** is converted, in less than 10 min, to the head-to-head *trans,anti,trans*-cyclobutane dimer **3** in 45% yield. The reaction appears to be completely (>99%) stereoselective, and as is customarily observed in cation radical processes catalyzed by **2**, the only noteworthy competing reaction is polymerization of **1**. Of somewhat greater mechanistic interest is the observation that dimerization of *trans*-**1** at −35 °C produces, instead of pure **3**, a 52:48 mixture of **3** and a second dimer (**4**), the latter being the same head-to-head *trans,syn,trans*-cyclobutane dimer produced in the direct photodimerization of 1.[5] Both **3** and the thermodynamically much less stable **4** are formed in reactions that are formally $[{}_{\pi}2_s + {}_{\pi}1_s]$ cycloadditions, i.e., with complete retention of the stereochemistry of *trans*-**1**, thus providing the first experimental suggestion of a possible stereospecific reaction. This premise was further examined by studying the cycloreversion of **4** to **1**, which occurs smoothly at 0 °C in methylene chloride solutions of **2**. GC/MS was used to analyze samples of the reaction quenched by methoxide/methanol at various stages of reaction, including times as short as 5 s. Even at the shortest reaction times, under conditions in which *cis*-**1** would have been readily detectable, the cycloreversion of **4** produces *trans*-**1** with complete (>99%) stereoselection. The subsequent dimerization of *trans*-**1** generates only **3** and, again, no other dimer. The cycloreversion of **4** is thus also a doubly suprafacial process, formally $[{}_{\pi}2_s + {}_{\pi}1_s]$, as would behoove a concerted cycloreversion, and is not accompanied by isomerization to any of the other possible cyclobutane dimers.

The dimerization of *cis*-anethole, which in theory should provide the most direct test of stereospecificity, was complex stereochemically, yielding (at 0 °C) **3**, **5**, and **6**, instead of pure **6** as expected for a selective $[{}_{\pi}2_s + {}_{\pi}1_s]$ cycloaddition. However, GC/MS analysis of the unreacted **1** revealed that the isomerization of *cis*-**1** to *trans*-**1** was occurring at a rate competitive with cycloaddition. Statistical treatment of product composition–time data (5–60 s) obtained by GC/MS analysis gave an extrapolated value for the percentage of **3** in the dimer mixture at zero time (no isomerization) of 0.0%. The dimerization *cis*-**1** thus yields none of the thermodynamically most stable dimer, within experimental error. These data strongly suggest that the dimerization

(1) Bell, F. A.; Crellin, R. A.; Fujii, N.; Ledwith, A. *Chem. Commun.* **1969**, 251.
(2) Ledwith, A. *Acc. Chem. Res.* **1972**, *5*, 133.
(3) Neunteufel, R. A.; Arnold, D. R. *J. Am. Chem. Soc.* **1973**, *95*, 4080.
(4) Bellville, D. J.; Wirth, D. D.; Bauld, N. L. *J. Am. Chem. Soc.* **1981**, *103*, 718.
(5) Nozaki, H.; Noyori, R.; Kawanisi, M. *Tetrahedron* **1968**, *24*, 2183.

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