A New Synthesis of Diazenes (Azoalkanes) Using 4-(*S,S*-Dimethylsulfoximino)-1,2,4-triazoline-3,5-dione. The Construction of Diazenes from Amino Nitrenes *via* Base-Induced Sulfoximine Cleavage

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Received January 2, 1997

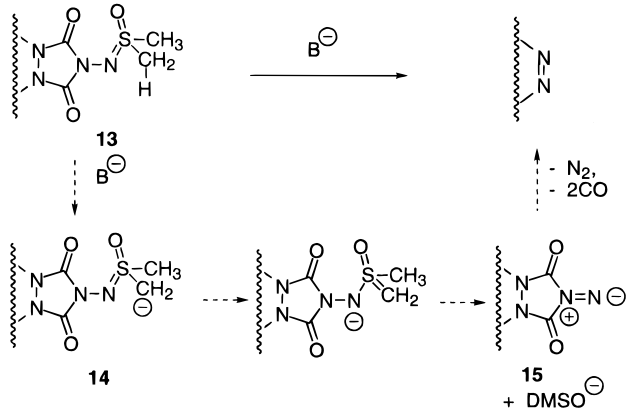
Diazenes are well known, valuable precursors of reactive intermediates.[1] They are most commonly prepared by the hydrolysis of either a biscarbamate or a urazole, followed by oxidation of the intermediate hydrazine or semicarbazide, respectively.[2] We describe the first synthesis and exploration of the chemistry of 4-(*S,S*-dimethylsulfoximino)-1,2,4-triazoline-3,5-dione (S-TAD, **1**). This material undergoes cycloaddition with conjugated dienes to afford urazoles in high yield and provides a useful and novel method for the construction of diazenes. The latter process is highlighted by a new, base-induced sulfoximine cleavage (**13** → **15**) that allows the *direct* conversion of urazole to diazene *via* the intermediacy of an aminonitrene (**15**), as illustrated in Scheme 1. Without isolation, the latter fragments to afford the diazene linkage, bypassing the oxidation step entirely.

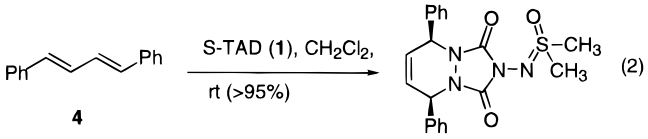
S-TAD (**1**) is easily synthesized from *N*-aminourazole (**2**, "p-urazine"),[3,4] a substance that can be prepared on a large scale *via* the self-condensation of semicarbazide hydrochloride. Thus, treatment of **2** with 2 equiv of iodobenzene diacetate (IBD, **3**) in DMSO converts the aminourazole to S-TAD (**1**). One equivalent of IBD (**3**) oxidizes the 1,2-hydrazide and the other oxidizes the resulting 1,1-hydrazide to the aminonitrene, which is subsequently intercepted by DMSO to form the sulfoximine.[5,6] S-TAD (**1**) is not isolated but is conveniently used as a solution in DMSO or acetonitrile.

(1)

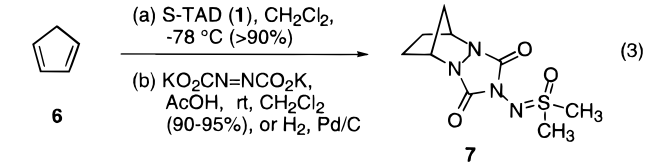
The cycloadditions are generally carried out at temperatures ranging from −78 °C to room temperature, depending, as illustrated in eqs 2 and 3, upon the reactivity of the cycloaddition partner.

Scheme 1. Proposed Pathway for Diazene Formation



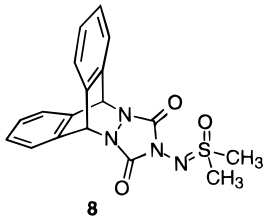


(2)



(3)

Once formed, the S-TAD adduct can be converted to the desired diazene by treatment with any of a variety of bases, aqueous potassium carbonate being particularly convenient; those bases found useful in the conversion of **8** to anthracene are illustrative.



8

conditions	yield (%, anthracene)
• 0.1 N K_2CO_3, 90 °C, 1 h	93-95
• pyrrolidine/H_2O, 90 °C	97
• pH 10 buffer, 85 °C, 3 h	93-95
• 0.1N Na_3BO_3, 90 °C, 24 h	90

Highlighting the utility of the methodology is its application to the synthesis of bicyclic diazenes that serve as precursors to the trimethylenemethane diradicals used in diyl trapping reactions (see Table 1).[2d,7] These materials are prepared *via* the reaction of S-TAD (**1**) with a fulvene such as **9a**−**c**, followed by reduction of the Δ-5,6

(1) (a) Adam, W.; De Lucchi, O. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 762. (b) Dougherty, D. A. *Acc. Chem. Res.* **1991**, *24*, 88. (c) Engel, P. S. *Chem Rev.* **1980**, 99.

(2) (a) Barton, D. H. R.; Shioiri, T.; Widdowson, D. A. *J. Chem. Soc., C* **1971**, 1968. (b) Semmelhack, M. F.; Foos, J. S.; Katz, S. *J. Am. Chem. Soc.* **1973**, *95*, 7325. (c) Squillacote, M.; De Felippis, J. *J. Org. Chem.* **1994**, *59*, 3564. (d) The diazenes illustrated in the table are known and their preparation is recorded in Little, R. D.; Carroll, G. L. *J. Org. Chem.* **1979**, *44*, 4720.

(3) Lenoir, J. A.; Colebrook, L. D.; Williams, D. F. *Can. J. Chem.* **1972**, *50*, 2661.

(4) N-Aminourazole was first synthesized by the Thiele and Curtius groups over a century ago. (a) Thiele, J.; Stange, O. *Liebigs Ann. Chem.* **1894**, *283*, 1. (b) Curtius, T.; Heidenreich, K. *Chem. Ber.* **1894**, 2684.

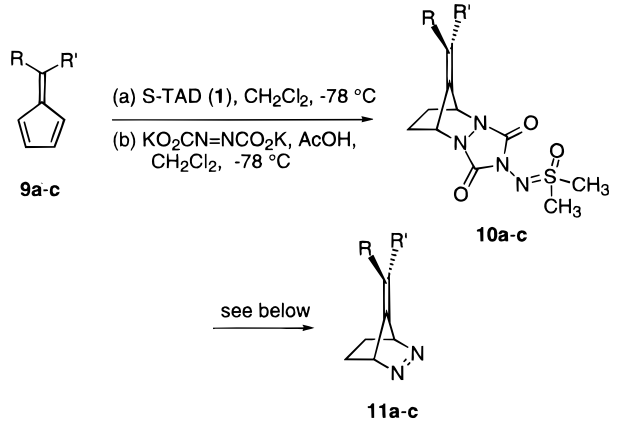
(5) (a) Cambell, C. D.; Rees, C. W. *Chem. Commun.* **1965**, *10*, 193. (b) Gilchrist, T. L.; Rees, C. W.; Stanton, E. *Chem. Commun.* **1971**, 801. (c) Anderson, D. J.; Horwell, D. C.; Stanton, E.; Gilchrist, T. L.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1317.

(6) The mechanism of hydrazine oxidation is not known. There is considerable evidence that a "free" amino-nitrene is not involved. The sulfoximine can be formed by the reaction of DMSO with another electrophilic nitrogen intermediates. See: (a) Atkinson, R. S.; Jones, D. W.; Kelly, B. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1344. (b) Atkinson, R. S.; Grimshire, M. J.; Kelly, B. J. *Tetrahedron* **1989**, *43*, 2873.

(7) Little, R. D. *Chem. Rev.* **1996**, *96*, 93.

S0022-3263(97)00011-X CCC: $14.00

Table 1. Diazene Formation from S-TAD Urazoles



	R	R′	yield %, **10**)	condns (**10** to **11**)	yield (%, **11**)
a	CH_3	CH_3	93	0.1 N K_2CO_3, 75 °C, 1.5 h	80
b	H	C_6H_4OMe-*p*	90	0.1 N K_3PO_4, 85 °C, 5 h	83
c	C_6H_5	C_6H_5	80	1 N K_2CO_3, 75 °C, 5 h	77

π bond of the resulting Diels−Alder adduct using diimide at low temperature.[8] The resulting highly polar products are readily characterized by the sulfoximine methyl singlet appearing at *ca.* 3.2 ppm of the ^{1}H NMR spectrum and the distinctive urazole signals found at 1715 and 1780 cm^{-1} in the IR.

Conversion of these materials to the corresponding diazene is a simple matter. For example, diazene **11a** was isolated in an 82% yield after stirring compound **10a** (200 mg, 0.66 mmol) dissolved in 40 mL of 1 N aqueous potassium phosphate at room temperature for 3 days.[2d] The reaction time was reduced, and a comparable yield (80%) was obtained when a 0.5 M solution of **10a** (100 mg, 0.33 mmol) was heated at 75 °C for 1.5 h in the presence of 0.1 N aqueous potassium carbonate. Because *cis*-diazenes are stabilized in water,[9] they can be generated at temperatures exceeding that required for extrusion of nitrogen in a nonaqueous solvent. This factor can prove advantageous in the synthesis of thermally labile diazenes. For example, while the diphenyl diazene **11c** has an estimated half-life of roughly 2 min at 75 °C in acetonitrile,[2d,10] it can be isolated in a 77% yield after treatment of urazole **10c** with aqueous potassium carbonate at that temperature for 5 h.

The mechanism for the conversion to diazene deserves comment. While the present reaction conditions call for the use of water as solvent, a hydrolytic pathway involving the attack of water or hydroxide on the carbonyl unit is not operable. Were that so, a stable semicarbazide intermediate would have formed; none could be detected. Instead, we favor the process portrayed in Scheme 1, one initiated by the removal of a proton from the dimethylsulfoximine unit of **13**. The feasibility of this pathway was demonstrated by showing that these protons are rapidly exchanged with deuterium when the process is conducted in the presence of D_2O and potassium carbonate. It is important to point out that the corresponding diphenylsulfoximine, *i.e.*, a system devoid of an abstractable proton, was *not* converted to diazene. Thus, it is reasonable to postulate a pathway involving deprotonation of **13**, followed by elimination of dimsylate to afford aminonitrene **15**, and its subsequent fragmentation with the extrusion of carbon monoxide and nitrogen to afford the diazene. In a sense, the process is reminiscent of the conversion of 1,1-disubstituted-2-arenesulfonohydrazides to aminonitrenes in the presence of base.[11]

In short, we have designed, synthesized, and examined the cycloaddition chemistry of a new triazolinedione, S-TAD (**1**). This material is particularly useful in its role as a precursor to diazenes. Of particular note is the fact that, under mildly basic conditions, S-TAD-derived urazoles undergo base-induced fragmentation, leading directly to the diazene unit.

Experimental Section

4-(*S,S*-Dimethylsulfoximino)-1,2,4-triazoline-3,5-dione (S-TAD, 1). Method A. Powdered *N*-aminourazole[3] (**2**, 0.116 g, 1.0 mmol) was dissolved in 5 mL of dry (3 Å mol sieves) DMSO and placed in a 25 mL flask cooled in a room-temperature water bath. Iodobenzene diacetate (IBD, **3**, 0.650 g, 2.0 mmol) was added in portions over 1 h. The slow addition of IBD prevented the decomposition of S-TAD (**1**) caused by overheating. The resulting deep violet colored solution of S-TAD (**1**; *ca.* 0.2 M) was used for cycloadditions: ^{1}H NMR (200 MHz, DMSO-d_6) δ 3.28 (s, 6 H, Me); ^{13}C NMR (200 MHz, DMSO-d_6) δ 222.59, 39.39; UV (DMSO) λ_{max} 310, 554 nm.

Method B. Powdered *N*-aminourazole[3] (**2**, 1.16 g, 10 mmol) was suspended in 10 mL of dry (3 Å mol sieves) DMSO. IBD (**3**, 3.22 g, 10 mmol) was added over 4 h to the ice-cooled suspension. The suspension was stirred at room temperature for 2 h. The solution remained violet throughout the reaction, slowly fading as S-TAD (**1**) was consumed. The reaction was considered complete when the solution was colorless and gave a negative test to starch−iodide paper; this indicated consumption of **3**. The suspension was triturated twice with 75 mL of ether to give 1.80 g (9.3 mmol, 93%) of dihydro-S-TAD: mp 220−221 °C (recrystallized from water); ^{1}H NMR (200 MHz, DMSO-d_6) δ 9.86 (s, 2 H), 3.19 (s, 6 H, Me); ^{13}C NMR (200 MHz, DMSO-d_6) δ 154.89, 40.35; IR (Nujol) 3245, 3010, 2938, 2900, 2851, 1687, 1432, 1374, 1328, 1218, 1189, 1043 cm^{-1}; MS (CI, CH_4) 79 (DMSO − H$^+$), 63, 44; MS (CI, NH_3) 193, 134, 96, 79; MS (CI, APCI) 193, 79 (100); HRMS (CI) calcd for $C_4H_9N_4O_3S$ 193.0395, found 193.0395 (MH$^+$).

Powdered dihydro-S-TAD (0.192 g, 1.0 mmol) and IBD (**3**, 0.330 g, 1.01 mmol) were suspended in 10 mL of MeCN. The suspension was stirred in the dark for 1 h to give a 0.1 M solution of S-TAD (**1**). No cooling bath was needed as the insolubility of both reactants moderated the reaction temperature. The reaction was judged to be complete when the solids had dissolved. This solution was used for the cycloaddition reactions.

General Procedure for the Diels−Alder Reactions of S-TAD (1) with Fulvenes. Formation of 10a−c. A solution of S-TAD (**1**) prepared via method B was added to 1 mmol of fulvene dissolved in 200 mL of CH_2Cl_2 precooled to −78 °C. The violet color of S-TAD (**1**) disappeared instantly upon addition. The reaction was complete when the solution remained faintly violet or when TLC indicated consumption of fulvene. Dipotassium azodicarboxylate (2.0 g, 10 mmol, 10 equiv) and glacial acetic acid (1.3 g, 20 mmol, 20 equiv) were added, and the solution was maintained at −78 °C for 4 h. The crude mixture was added to a 2.5 × 2.5 cm plug of silica and eluted with ether; organic byproducts elute first. Further elution with 10% MeOH

(8) Fulvene adducts with STAD (**1**) must be hydrogenated at low temperature using diimide to avoid rearrangements. Attempts to convert the initially formed adduct to diazene *without* first reducing the Δ-5,6 π bond would afford an unstable material that would lose nitrogen and regenerate the fulvene. (a) Adam, W.; Erden, I. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 210. (b) Olsen, H. *Angew. Chem. Suppl.* **1982**, 893. (c) Zhang, X.; Khan, S. I.; Foote, C. S. *J. Org. Chem.* **1995**, *60*, 4102. Adducts that do not rearrange can be conveniently hydrogenated over Pd/C.

(9) Little, R. D.; Brown, L. M. *J. Am. Chem. Soc.* **1992**, *114*, 3071 and references therein.

(10) Little, R. D.; Billera, C. B. *Tetrahedron Lett.* **1988**, *29*, 5711.

(11) See also, (a) Carpino, L. A. *J. Am. Chem. Soc.* **1957**, *79*, 4427. (b) Carpino, L. A.; Göwecke, S. *J. Org. Chem.* **1964**, *29*, 2824. (c) Carpino, L. A. *J. Org. Chem.* **1965**, *30*, 737.

in CH_2Cl_2 and concentration *in vacuo* afforded the hydrogenated cycloadduct **10**. Spectral data for compounds **10a**−**c** follow.

4-(*S,S*-Dimethylsulfoximino)-10-(isopropylidine)-2,4,6-triaza[5.2.2.0^{2,6}]-tricyclodecane-3, 5-dione (10a): 80% yield; mp 190−194 °C (recrystallized from CH_2Cl_2/pentane); TLC (10% MeOH/CH_2Cl_2) R_f 0.35, stains blue with *p*-anisaldehyde; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.70 (s, 2 H), 3.16 (s, 6 H, Me), 1.88 (m, 4 H), 1.64 (s, 6 H, Me); ^{13}C NMR (200 MHz, $CDCl_3$) δ 159.4, 131.8, 124.0, 59.5, 40.6, 27.7, 20.9; IR ($CDCl_3$) 3027, 2982, 2935, 2862, 1771, 1719, 1383, 1229, 1184, 909, 728 cm^{-1}; MS (EI) 298, 220, 192, 134, 107, 93, 79 (100), 63; MS (CI, NH_4) 299 (100), 221, 208, 193, 107, 96, 79; MS (APCI) 299 (100), 221, 193, 107, 79; HRMS (EI) calcd for $C_{12}H_{18}N_4O_3S$ 298.1099, found 298.1096.

4-(*S,S*-Dimethylsulfoximino)-10-(4-methoxybenzylidene)-2,4,6-triaza[5.2.2.0^{2,6}]tricyclodecane-3, 5-dione (10b): 83% yield; mp 146−150 °C; TLC (10% MeOH/CH_2Cl_2) R_f 0.4, stains blue with *p*-anisaldehyde; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.11 (d, 8.7 Hz, 2 H), 6.81 (d, 8.7 Hz, 2H), 6.36 (s, 1 H), 5.1 (s, 1 H), 4.58 (s, 1 H), 3.72 (s, 3 H, Me), 3.12 (s, 3 H, Me), 3.06 (s, 3 H, Me), 2.0 (m, 4 H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 159.5, 159.4, 136.6, 129, 127, 120, 119, 114, 77.2, 63.7, 58.7, 55.1, 40.4, 40.2, 27.4; IR ($CDCl_3$) 3013, 2358, 1769, 1714, 1604, 1509, 1382, 1218, 1029 cm^{-1}; MS (CI, NH_3) 377, 286, 185, 79 (100); HRMS (CI) calcd for $C_{17}H_{21}N_4O_4S$ 377.1283, found 377.1270 (MH^+).

4-(*S,S*-Dimethylsulfoximino)-10-(diphenylmethylidene)-2,4,6-triaza[5.2.2.0^{2,6}]tricyclodecane-3, 5-dione (10c): 77% yield; mp 214−216 °C (recrystallized from MeOH); TLC (10% MeOH/CH_2Cl_2) R_f 0.35, stains blue with *p*-anisaldehyde; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.35 (m, 3 H, 7.15 (m, 2 H), 4.89 (s, 2 H), 3.23 (s, 6 H, Me) 2.11 (m, 4 H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 158.9, 136.5, 134.5, 129.3, 128.4, 128.2, 61.0, 41.0, 27.9; IR ($CDCl_3$) 3018, 1773, 1708, 1380, 1210, 1033 cm^{-1}; MS (CI, NH_3) 423, 274, 231 (100), 193, 96, 79; HRMS (EI) calcd for $C_{22}H_{23}N_4O_3S$ 423.1490, found 422.1424.

General Procedure for the Diels−Alder Reactions of S-TAD (1) with Unreactive Dienes: Anthracene and 1,4-Diphenylbutadiene (4). Preparation of 5 and 8. A 1 mmol solution of S-TAD (**1**), prepared by method B, was added to 1 mmol of diene dissolved in 50 mL of CH_2Cl_2 at room temperature. When the solution was no longer violet, the crude mixture was added to a 2.5 × 2.5 cm plug of silica and washed with ether (100 mL) to remove organic byproducts. Further elution with 50 mL of 10% MeOH/CH_2Cl_2 and concentration *in vacuo* afforded the adduct in 90−100% purity, as determined by ^{1}H NMR. The adducts were recrystallized from MeOH. Spectral data and melting points for **5** and **8** are presented below.

2,5-Diphenyl-8-(*S,S*-dimethylsulfoximino)-1,6,8-triaza-[4.3.0]bicyclonon-3-ene-7,9-dione (5): mp 224−226 °C (recrystallized from MeOH); TLC (10% MeOH/CH_2Cl_2) R_f 0.35, stains blue with *p*-anisaldehyde; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.47 (m, 4 H), 7.36 (m, 6H), 5.96 (s, 2 H), 5.47 (s, 2 H), 3.10 (s, 6 H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 154, 137.1, 128.7, 128.5, 127.8, 125.2, 58.1, 40.8; IR ($CDCl_3$) 3013, 2356, 1773, 1710, 1602, 1411, 1210, 1085 cm^{-1}; MS (CI, NH_3) 397, 321, 306, 235 (diazenium cation), 206, 79 (100); HRMS (EI) calcd for $C_{20}H_{21}N_4O_3S$ 396.1256, found 396.1258.

8,9:10,11-Dibenzo-4-(*S,S*-dimethylsulfoximino)-2,4,6-triaza[5.2.2.0^{2,6}]tricycloundeca-8,10-diene-3,5-dione (8): mp 230−234 °C (recrystallized from MeOH); TLC (10% MeOH/CH_2Cl_2) R_f 0.45, stains brown with *p*-anisaldehyde; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45 (m, 4H), 7.26 (m, 4H), 6.23 (s, 2 H), 2.95 (s, 6H); ^{13}C-NMR (DMSO-d_6) δ 157, 136.5, 127.9, 124.0, 59.4, 39.0; IR ($CDCl_3$) 3014, 2919, 2256, 1760, 1706, 1455, 1380, 1199, 1124, 1025, 904, 734 cm^{-1}; UV (MeCN) λ_{max} 212, 262 nm; MS (CI, CH_4) 207 (protonated diazenium cation), 179, 178 (anthracene, 100), 79 (DMSO − H^+), 44; HRMS (CI) calcd for $C_{18}H_{15}N_4O_3S$ 369.1021, found 369.1028 (MH^+).

Base-Induced Sulfoximine Cleavage of Adduct 8. Using Potassium Carbonate. Adduct **8** (220 mg, 0.59 mmol) was suspended in 300 mL of 0.1 N K_2CO_3 and heated to 90 °C for 1 h. The fluorescence of anthracene could be seen in the flask (long wavelength UV) immediately after heat was applied. The reaction mixture was added to 20 mL of brine and extracted twice with 20 mL of CH_2Cl_2. The organic layer was dried over Na_2SO_4, concentrated, and chromatographed on silica gel, eluting with ether. Removal of the solvent afforded 97 mg (0.54 mmol, 92%) of anthracene.

Using Pyrrolidine. Adduct **8** (20 mg, 0.05 mmol) was suspended in 4 mL of H_2O and 1 mL of pyrrolidine and heated at 90 °C for 3 h. The reaction mixture was cooled, quenched with 20 mL of 0.1 N HCl, and worked up as described above to give 9.4 mg (0.047 mmol, 97%) of anthracene.

Using pH 10 Buffer. Adduct **8** (20 mg, 0.05 mmol) was suspended in 3 mL of Fisherbrand pH 10 buffer and heated at 90 °C for 3 h. After standard workup (see above), 9−9.2 mg (0.045−0.046 mmol, 93−95%) of anthracene was obtained.

Using Na_3BO_3. Adduct **8** (20 mg, 0.05 mmol) was dissolved in 3 mL of 0.1 N Na_3BO_3 and heated at 90 °C for 24 h. After standard workup (see above), 9 mg (0.045 mmol, 90%) of anthracene was obtained.

Diradical Precursors 11a−c. These materials are known.[2d] Adduct **10a** (100 mg, 0.33 mmol) was dissolved in 500 mL of 0.1 N K_2CO_3 and heated at 75 °C for 1.5 h. The aqueous layer was extracted with CH_2Cl_2 and the organic layer dried over Na_2SO_4 and concentrated *in vacuo* to afford 73 mg (82%) of diazene **11a**. Adduct **10b** (50 mg, 0.13 mmol) was heated in 50 mL of 0.1 M aqueous K_3PO_4 at 85 °C for 3 h. Workup as previously described afforded 25 mg of diazene **11b** (0.1 mmol, 83%). Adduct **11c** (50 mg, 0.12 mmol) was heated in 80 mL of 1.0 M aqueous K_2CO_3 at 75 °C for 5 h. Workup as previously described afforded 23 mg of diazene **11c** (0.9 mmol, 77%).

Acknowledgment. We are grateful to the National Science Foundation and the National Institutes of Health for their support of our research programs.

Supporting Information Available: ^{1}H and ^{13}C NMR data for dihydro-S-TAD and S-TAD (**1**) in DMSO-d_6, as well as for compounds **5**, **8**, and **10a**−**c** (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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