Bis- and Tris(tetrathiafulvalenes) (TTFs) Derived from Reactions of the TTF-thiolate Anion

Martin R. Bryce,* Gary J. Marshallsay, and Adrian J. Moore

Department of Chemistry, University of Durham, Durham DH1 3LE, U.K.

Received March 30, 1992

A range of new bis- and tris-TTF derivatives has been prepared using the TTF-thiolate anion **2** as a key intermediate. Thiolate anion **2** reacts with 2-bromoethanol to yield alcohol **3** from which the bis- and tris-TTF systems **4–7** have been obtained by reaction with the appropriate acid chloride. Subsequent reactions of the malonate anion of dimeric TTF **7** yield derivatives **8–10**, which include the amphiphilic system **8**. Thiolate anion **2** reacts with bis- and tris(bromomethyl)benzene to yield bis- and tris-TTF derivatives **11** and **12**, respectively. Thioester **13**, which serves as a shelf-stable precursor of thiolate anion **2**, has been used in the synthesis of bis-TTF systems **17** and **18**. The solution electrochemistry of the new multi-TTF derivatives has been studied by cyclic voltammetry, which reveals that the TTF moieties do not interact to any significant extent.

Introduction

In the search for new electron donors suitable for the formation of conducting charge-transfer complexes ("organic metals"),[1] covalently linked dimers, and higher multiples of tetrathiafulvalene (TTF, **1**) are challenging synthetic targets.[2] Both the structural and electronic properties of such systems are of interest. For example, by varying the linking group it is possible to control the relative juxtaposition of neighboring TTF units in the crystal structure,[3] and this may be a way of modifying the band filling in derived salts.[2g] The solution electrochemical properties of some covalently tethered TTFs are considerably more complex than monomeric TTFs, probably due to a combination of both inter- and intramolecular interactions.[2g,m]

We have developed the high reactivity of the TTF-thiolate anion **2** for covalently linking TTF units via a range of spacer groups. *This approach to multi-TTF systems is quite distinct from previously reported routes*[2] and has provided the unsymmetrical dimer **4**, the symmetrical dimers **6**, **7**, **11**, **17**, and **18**, and the trimers **5** and **12**. Further functionalization of dimer **7**, by reactions at the central methylene group, is also reported.

Results and Discussion

Synthesis of Bis- and Tris-TTF Derivatives. Monolithiation of TTF (**1**), under standard conditions,[4] followed by addition of elemental sulfur, affords the intermediate TTF-thiolate anion **2**, which can be trapped with 2-bromoethanol to yield compound **3**.[5] We have exploited the reactivity of the alcohol group of **3** with acid chlorides in the presence of triethylamine to obtain bis- and tris-TTF systems in which the TTF moieties are joined through ester linkages. TTF-carbonyl chloride, which was prepared from TTF-carboxylic acid[6] and used without purification, reacted with alcohol **3** to yield the first unsymmetrical bis-TTF derivative **4** in 34% yield (based on TTF-carboxylic acid). Similarly, 3-fold reaction of **3** with benzene-1,3,5-tris(carbonyl chloride) yielded the tris-TTF system **5** (72%). Reaction of compound **3** with triphosgene gave compound **6** (78%), and reaction with malonyl dichloride gave the symmetrical malonate ester derivative **7** (84%).

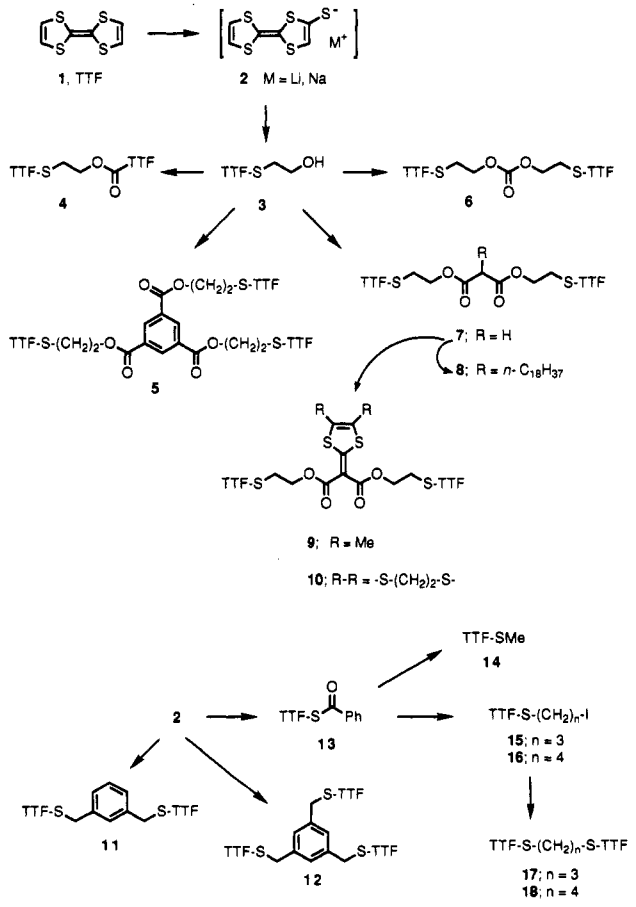

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Table I. Cyclic Voltammetric Data for TTF Derivatives Reported in Volts vs Ag/AgCl, in Dichloromethane under Argon, Pt Button Electrode, Pt Wire Counter Electrode, ca. 5×10^{-4} M Compound, 0.1 M $Bu_4N^+PF_6^-$, Scan Rate 100 mV s^{-1}, Recorded on a BAS 100 Electrochemical Analyzer. Data for TTF 1 Are Provided for Reference

compd	$E_1^{1/2}$	$E_2^{1/2}$
1 (TTF)	0.34	0.71
3	0.41	0.81
4	0.45, 0.56	0.79
5	0.45	0.78
6	0.46	0.81
7	0.47	0.78
8	0.47	0.79
9[a]	0.44	0.81
10[a]	0.43	0.81
11	0.45	0.79
12	0.47	0.81
13	0.45	0.81
14	0.42	0.80
15	0.46	0.86
16	0.44	0.81
17	0.44	0.78
18	0.44	0.81

[a] Additionally for compounds 9 and 10, E_3^{ox} 1.45 and 1.26 V, respectively.

Compound 7 is a particularly versatile bis-TTF derivative, as further functionalization of the central malonate methylene group can be readily achieved by deprotonation with sodium hydride, followed by addition of electrophiles. Accordingly, reaction of the anion of 7 with 1-iodooctadecane gave compound 8 (62%), and reaction with the appropriate 2-(methylthio)-1,3-dithiolium iodide derivatives afforded compounds 9 and 10, respectively, in 88–91% yields. The amphiphilic compound 8 has been synthesized to explore the incorporation of bis-TTF derivatives into Langmuir–Blodgett film structures,[2m,7] while compounds 9 and 10 were prepared to obtain crystalline derivatives for characterization and to demonstrate that additional 1,3-dithiole rings capable of one-electron oxidation can be incorporated into the structure. TTF-thiolate anion 2 has also been trapped with 1,3-bis(bromomethyl)benzene and 1,3,5-tris(bromomethyl)benzene to yield the bis- and tris-TTF derivatives 11 and 12, respectively, in 10–17% yields. Reaction of thiolate anion 2 with benzoyl chloride gave thioester 13 (70–78% yield) from which the thiolate anion 2 can be efficiently regenerated (as the sodium salt) by treatment with sodium ethoxide in ethanol at −10 °C; this was established by trapping anion 2, generated in this way, with iodomethane, which gave 4-(methylthio)TTF 14 in 96% yield. The same reaction at room temperature gave compound 14 in only 41% yield. Benzoyl thioester 13 serves, therefore, as a convenient shelf-stable equivalent of the TTF-thiolate anion.[8]

Addition of thiolate anion 2, generated from reagent 13, to an excess of 1,3-diiodopropane and 1,4-diiodobutane yielded iodides 15 and 16, respectively, in 43–50% yields. Reaction of iodides 15 and 16 with a second equivalent of thiolate anion 2 (also generated from thioester 13) proceeded less efficiently to provide the bis-TTF systems 17 and 18, respectively (11–26% yields). This two-step route was more efficient than one-pot syntheses of 17 and 18 (from 2 equiv of thiolate 2 and 1 equiv of diiodoalkane) which proceeded in only ca. 5% yield.

Electrochemical Studies. The electrochemical redox properties of all the new TTF derivatives described herein have been investigated by cyclic voltammetry; these data, along with those of the reference compound TTF 1, are collated in Table I. The monomeric TTF derivatives 3 and 13–16 display two, reversible, single-electron oxidation waves, typical of the TTF system. Predictably, the values of E_1 and E_2 are raised slightly by the alkylthio substituent.[2m,9] The symmetrical dimers 6–11, 17, and 18 and the symmetrical trimers 5 and 12 each show two reversible redox waves at very similar potentials to the monomers, due to simultaneous oxidation of the two or three TTF units at the same potentials. Thus, the dimers sequentially form dications and tetracations, and the trimers form trications and hexacations, with no intermediate oxidation states being detected. There is no apparent broadening of either of the two oxidation waves, suggesting that there are no inter- or intramolecular Coulombic repulsion effects between charged TTF moieties and that the individual TTF units are electronically isolated by the spacer groups and do not interact to any significant extent. Previous workers on bis-TTF systems have observed intermolecular effects in cyclic voltammetric studies, but only when shorter spacer groups,[2m] or single atoms,[2d,k,l,p] are bridging the TTF units.

Compounds 9 and 10 show an additional third oxidation step which is irreversible; this is a one-electron oxidation of the central 1,3-dithiol-2-ylidene ring to form the 1,3-dithiolium cation. Notably, this oxidation occurs at a higher potential (by ca. 0.2 V) for compound 9 than for compound 10; this clearly implies that the ethylenedithio bridge of the latter compound acts as an electron-donating substituent on the 1,3-dithiol-2-ylidene ring, in marked contrast to its electron-withdrawing effect when fused to the TTF framework.[9,10] For the unsymmetrical dimer 4, three distinct redox waves are observed. The values of E_1 (each representing a one-electron, neutral → cation-radical redox process for a TTF moiety) are now separated by 0.11 V, which is consistent with the known higher oxidation potential of ester-substituted TTF derivatives[11] compared to alkylthio analogues. It is unlikely that this splitting of E_1 is due to intramolecular Coulombic effects, as the two TTF rings of compound 4 are separated by a five-atom bridge[2m] (cf. data for compound 17, which also has a five-atom bridge). The second oxidations of both of the TTF rings of dimer 4 (to form the tetracation species) are observed as a single, two-electron wave.

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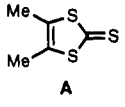
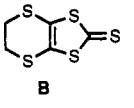
(10) To investigate further this interesting effect we have measured the oxidation potentials of the corresponding thiones A and B, under the conditions reported in Table I. These compounds are oxidized at the same potentials as E_3^{ox} for compounds 9 and 10, respectively, showing that compound B is the stronger donor.



A



B

(11) The values of $E_1^{1/2}$ and $E_2^{1/2}$ for TTF–$CO_2C_6H_{13}$ are 0.51 and 0.87 V. Bryce, M. R.; Moore, A. J. Unpublished results.

Experimental Section

General Details. Details of instrumentation have been reported recently.[12]

Generation and Trapping of TTF-thiolate Anion 2: General Procedure. Preparation of Compounds 3 and 13. Into a stirred solution of TTF (1) (2.0 g, 10 mmol) in dry ether (125 mL) at −78 °C under nitrogen was syringed a freshly-prepared solution of LDA [obtained from diisopropylamine (1.5 mL, 11 mmol) and *n*-butyllithium (1.6 M, 6.74 mL, 11 mmol) in dry ether (15 mL) at −78 °C] over a period of 10 min. A yellow precipitate of monolithiated-TTF began to form after ca. 10 min, and stirring was continued for a further 45 min at −78 °C. Elemental sulfur (0.47 g, 15 mmol) was then added in one portion against a positive pressure of nitrogen, and stirring was continued at −78 °C for 7 h, after which time either 2-bromoethanol (1.4 mL, 20 mmol) or benzoyl chloride (2.3 mL, 20 mmol) was syringed into the slurry over 5 min. The mixture was stirred at −78 °C for 2 h and then slowly warmed to 20 °C over 12 h. Water (120 mL) was added and the mixture extracted into dichloromethane (4 × 100 mL), the combined extracts were washed with water (100 mL) and dried ($MgSO_4$), and the solvent was evaporated in vacuo. Chromatography of the residue on a silica column eluting first with hexane/dichloromethane (4:1 v/v) gave unreacted TTF (1) (ca. 400 mg, 20%) then with dichloromethane afforded the product. There were obtained the following:

Compound 3: a yellow solid; 2.06 g (75%); mp 101–102 °C (from dichloromethane/cyclohexane); MS (EI) *m/e* 280 (M^+); NMR (δ_H, $CDCl_3$) 6.43 (s, 1 H), 6.32 (s, 2 H), 3.80 (t, 2 H, J = 5.9 Hz), 2.93 (t, 2 H, J = 5.9 Hz), and 2.07 (broad s, 1 H). Anal. Calcd for $C_6H_8OS_5$: C, 34.3; H, 2.9. Found: C, 34.4; H, 2.8.

Compound 13: an orange solid; 2.61 g (78%); mp 126–127 °C (from dichloromethane/cyclohexane); MS (DCI) *m/e* 341 (M^+ + 1); NMR (δ_H, $CDCl_3$) 7.93 (2 H, m), 7.63 (1 H, m), 7.48 (2 H, m), 6.60 (1 H, s), and 6.32 (2 H, s). Anal. Calcd for $C_{13}H_8OS_5$: C, 45.8; H, 2.4. Found: C, 45.6; H, 2.2.

Preparation of Compounds 11 and 12. Reaction conditions and molar ratios were identical with those described above for the preparation of compounds 3 and 13, except that the procedure was carried out using TTF (1) (500 mg, 2.5 mmol) and either 1,3-bis(bromomethyl)benzene (320 mg, 1.21 mmol) or 1,3,5-tris-(bromomethyl)benzene (175 mg, 0.49 mmol). There were obtained the following:

Compound 11: a yellow solid; 70 mg (10%); mp 73–75 °C (from ether/methanol); MS (DCI) *m/e* 575 (M^+ + 1); NMR (δ_H $CDCl_3$) 7.28–7.13 (4 H, m), 6.30 (4 H, s), 6.11 (2 H, s), and 3.89 (4 H, s). Anal. Calcd for $C_{20}H_{14}S_{10}$: C, 41.8; H, 2.5. Found: C, 41.4; H, 2.3.

Compound 12: an orange solid; 70 mg (17%); mp 49–52 °C (from ether/methanol); NMR (δ_H $CDCl_3$) 7.06 (3 H, s), 6.32 (6 H, s), 6.13 (3 H, s), and 3.86 (6 H, s). Anal. Calcd for $C_{27}H_{18}S_{15}$: C, 39.4; H, 2.2. Found: C, 39.1; H, 2.1.

Preparation of TTF Esters 4–7: General Procedure. Preparation of Compounds 4–7. Into a solution of alcohol 3 (100 mg, 0.35 mmol) and the appropriate acid chloride (see below) in dry dichloromethane (25 mL) at 20 °C under nitrogen was syringed triethylamine (0.5 mL, 0.35 mmol) in one shot. The mixture was stirred at 20 °C for 3 h, and then water (50 mL) was added and the mixture extracted with dichloromethane (2 × 25 mL). The combined extracts were washed with water, dried ($MgSO_4$), and evaporated. Chromatography of the residue on a silica column eluting with cyclohexane/dichloromethane (1:1 v/v) afforded the product esters. There were obtained the following:

Compound 4: [from TTF-carbonyl chloride which was prepared[6] from TTF-carboxylic acid (90 mg)[4] and used without purification] a red solid; 62 mg (34%, based on TTF-carboxylic acid); mp 91–93 °C (from ether/methanol); MS (EI) 510 (M^+); NMR (δ_H, $CDCl_3$) 7.32 (1 H, s), 6.47 (1 H s), 6.31 (2 H, broad s), 4.42 (2 H, t, J = 5.8 Hz), and 3.03 (4 H, t, J = 5.8 Hz). Anal. Calcd for $C_{15}H_{10}O_2S_9$: C, 35.3; H, 2.0. Found: C, 35.5, H, 2.1.

Compound 5: [from benzene-1,3,5-tris(carbonyl chloride) (32 mg, 0.12 mmol)] a yellow solid; 85 mg (72%); mp 60–61 °C (from ether/methanol); MS, M^+ not observed; NMR (δ_H, $CDCl_3$) 8.79 (3 H, s), 6.48 (3 H, s), 6.27 (6 H, 3 equiv of AB, J_{AB} = 6.6 Hz), 4.61 (6 H, t, J = 6.1 Hz), and 3.16 (6 H, t, J = 6.1 Hz). Anal. Calcd for $C_{33}H_{24}O_6S_{15}$: C, 39.7; H, 2.4. Found: C, 39.9; H, 2.7.

Compound 6: [from triphosgene (17 mg, 0.06 mmol)] an orange oil; 81 mg (78%); MS, M^+ not observed; NMR (δ_H, $CDCl_3$) 6.47 (2 H, s), 6.32 (4 H, s), 4.32 (4 H, t, J = 6.4 Hz), and 3.00 (4 H, t, J = 6.4 Hz).

Compound 7: [from malonyl dichloride (24 mg, 0.17 mmol)] an orange oil; 94 mg (84%); MS, M^+ not observed; NMR (δ_H, $CDCl_3$) 6.47 (2 H, s), 6.33 (4 H, s), 4.34 (4 H, t, J = 6.4 Hz), 3.43 (2 H, s), and 2.99 (4 H, t, J = 6.3 Hz).

Preparation of Compounds 8–10: General Procedure. Compound 7 (100 mg, 0.16 mmol) was dissolved in dry THF (40 mL) under nitrogen at 20 °C, and to this solution was added sodium hydride (60% dispersion in mineral oil, 7.6 mg, 0.19 mmol) in one portion. The mixture was stirred at 20 °C for 2 h, and then either *n*-octadecyl iodide or the appropriate 1,3-dithiolium cation salt (0.17 mmol) was added in one portion and stirring was continued at 20 °C for 12 h. The solvent was then removed in vacuo, water was added, and the mixture was extracted with dichloromethane (2 × 25 mL). The combined extracts were dried ($MgSO_4$), filtered, and evaporated. Chromatography of the residue on a silica column eluted with cyclohexane/dichloromethane (1:1, v/v) gave the product. There were obtained the following:

Compound 8: [from *n*-octadecyl iodide (60 mg, 0.17 mmol)] a viscous yellow oil; 87 mg (62%); MS, M^+ not observed; NMR (δ_H, $CDCl_3$) 6.46 (2 H, s), 6.32 (4 H, s), 4.34 (4 H, t, J = 6.3 Hz), 3.38 (1 H, t, J = 7.5 Hz), 2.98 (4 H, t, J = 6.3 Hz), 1.87 (2 H, m), and 1.42–1.25 (35 H, m).

Compound 9: [from 2-(methylthio)-4,5-dimethyl-1,3-dithiolium iodide[12] (50 mg, 0.17 mmol)] a yellow solid; 109 mg (91%); mp 138–139 °C (from dichloromethane/cyclohexane); MS, M^+ not observed; NMR (δ_H, $CDCl_3$) 6.45 (2 H, s), 6.31 (4 H, s), 4.43 (4 H, t, J = 6.2 Hz), 3.10 (4 H, t, J = 6.2 Hz), and 2.20 (6 H, s). Anal. Calcd for $C_{24}H_{20}O_4S_{12}$: C, 38.0; H, 2.7. Found: C, 37.9; H, 2.9.

Compound 10: [from 2-(methylthio)-5,6-dihydro-1,3-dithiolo[4,5-*b*][1,4]dithiin-2-ium tetrafluoroborate[13] (52 mg, 0.17 mmol)] a yellow solid; 115 mg (88%); mp 67–68 °C (from dichloromethane/cyclohexane); MS, M^+ not observed; NMR (δ_H, $CDCl_3$) 6.44 (2 H, s), 6.30 (4 H, s), 4.43 (4 H, t, J = 6.4 Hz), 3.35 (4 H, s), and 3.09 (4 H, t, J = 6.4 Hz). Anal. Calcd for $C_{24}H_{18}O_4S_{14}$: C, 35.1; H, 2.2. Found: C, 35.0; H, 2.4.

Preparation of Compounds 14–16: General Procedure. A suspension of thioester 13 (200 mg, 0.59 mmol) in dry ethanol (100 mL) was cooled to −10 °C under nitrogen, sodium ethoxide (4.6 mL of an 0.14 M solution in dry ethanol) was added, and the mixture was stirred for 0.5 h at −10 °C. This solution was then added dropwise to an excess of the electrophile (either methyl iodide, 1,3-diiodopropane, or 1,4-diiodobutane) over a period of 0.5 h. The reaction mixture was stirred at −10 °C for 2 h and then allowed to warm to room temperature. Ethanol was then removed in vacuo, water was added, and the mixture was extracted into dichloromethane. The organic layer was dried ($MgSO_4$) and evaporated. The residue was chromatographed on a silica column, with cyclohexane/toluene (3:1 v/v) as the eluent, to yield the product. There were obtained the following:

Compound 14: an orange oil; 142 mg (96%); MS (DCI) 251 (M^+ + 1); NMR (δ_H, $CDCl_3$) 6.32 (2 H, s), 6.28 (1 H, s), and 2.39 (3 H, s).

Compound 15: a yellow oil; 120 mg (50%); MS (DCI) 405 (M^+ + 1); NMR (δ_H, $CDCl_3$) 6.38 (1 H, s), 6.32 (2 H, s), 3.28 (2 H, t, J = 6.8 Hz), 2.85 (2 H, J = 6.9 Hz), 2.11 (2 H, pentet, J = 6.8 Hz).

Compound 16: a yellow oil; 106 mg (43%); MS (DCI) 419 (M^+ + 1); NMR (δ_H, $CDCl_3$) 6.37 (1 H, s), 6.32 (2 H, s), 3.19 (2 H, t, J = 6.8 Hz), 2.76 (2 H, t, J = 7.1 Hz), 1.93 (2 H, m), and 1.74 (2 H, m).

Preparation of Compounds 17 and 18: General Procedure. To a solution of the sodium thiolate salt 2, generated from thioester 13 (100 mg, 0.29 mmol) as described above for compounds 14–16, was added either TTF derivative 15 (120 mg, 0.30 mmol) or 16 (125 mg, 0.30 mmol). The mixture was stirred under

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nitrogen at -10 °C for 2 h and then allowed to warm to 20 °C overnight. Aqueous workup as described for compounds 14-16, followed by column chromatography on silica, eluent cyclohexane/toluene (3:1 v/v), gave the products. There were obtained the following:

Compound 17: an orange oil: 40 mg (26%); MS (DCI) 513 ($M^+ + 1$); NMR (δ_H, $CDCl_3$) 6.39 (2 H, s), 6.32 (4 H, s), 2.83 (4 H, t, J = 7.0 Hz), and 1.95 (2 H, pentet, J = 7.0 Hz).

Compound 18: an orange solid: 17 mg (11%); mp 124-126 °C; MS (DCI) 527 ($M^+ + 1$); NMR (δ_H, $CDCl_3$) 6.36 (2 H, s), 6.32 (4 H, s), 2.75 (4 H, m), and 1.74 (4 H, m). Anal. Calcd for $C_{16}H_{14}S_{10}$: C, 36.5; H, 2.7. Found: C, 36.3; H, 2.5.

Acknowledgment. This work was funded by SERC.

A Theoretical Study of Intramolecular Diels-Alder and 1,3-Dipolar Cycloaddition Stereoselectivity Using ab Initio Methods, Semiempirical Methods, and a Tandem Quantum Mechanic-Molecular Mechanic Method

Frank K. Brown*

Glaxo Research Institute, Five Moore Drive, Research Triangle Park, North Carolina 27709

U. Chandra Singh and Peter A. Kollman

Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, San Francisco, California 94143

Laura Raimondi and K. N. Houk

Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California 90024

Charles W. Bock

Department of Chemistry, Philadelphia College of Textiles and Science, Philadelphia, Pennsylvania 19144

Received April 14, 1992

Diels-Alder and nitrile oxide intramolecular cycloadditions were studied using several methods. The structures found using all methods are similar when the forming bonds lengths are constrained, but the stereochemical predictions are quite different. The experimental stereochemical differences found for the parent Diels-Alder reactions forming 6-5 and 6-6 systems are rationalized. When the addends are linked by three methylene groups (formation of a five-membered ring), the strain in the transition structure (TS) causes the addends to twist about the forming bonds, resulting in a skewed TS as compared to the intermolecular TS. However, when the addends are linked by four methylene groups (formation of a six-membered ring), there is little strain in the TS, and the addends do not twist.

Introduction

The primary goal of this investigation was to determine the origins of the stereochemical preferences found for intramolecular nitrile oxide (INOC) and Diels-Alder (IDA) cycloadditions. This was accomplished by locating transition structures for the parent systems. The secondary goal was to determine a method for locating these transition structures that will satisfy both the necessary requirements for accuracy and cost. To do this, a tandem quantum mechanics (QM)/molecular mechanics (MM) methodology was evaluated. Interest in the intramolecular Diels-Alder cycloadditions arises from the wealth of available experimental results[1,2] and the utility of this type of reaction in synthesis. For two decades this reaction has been used for the formation of the hydrindan (5-6) and decalin (6-6) ring systems in the synthesis of natural products. The stereoselectivity of the 1,3,8-nonatrienes differs considerably from that of the 1,3,9-decatrienes depending on the substitution pattern (Table I). The study also included several examples of intramolecular nitrile oxide cycloadditions. This reaction is used for the synthesis of five- and six-membered rings fused to the heterocyclic isoxazoline ring.[3] Here no stereoisomers are possible in the absence of substituents, but the degree of flexibility of the forming five-membered ring will influence the stereoselectivity in substituted cases.

Both types of cycloadditions have been scrutinized previously[4] through the use of QM and MM. The previous approach involved QM to determine the intermolecular transition structure (TS) of the reaction and parameters

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