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symm-Tetramethylenecyclooctane: En Route to Polyspirocycles

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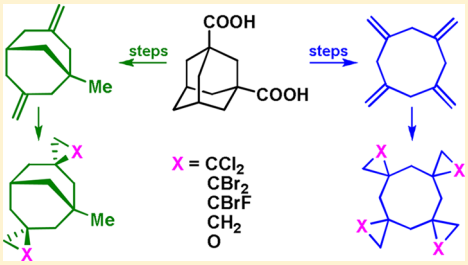
Supporting Information

ABSTRACT: A straightforward gram-scale synthesis of 1,3,5,7-tetrakis(methylidene)cyclooctane (TMCO) from commercial adamantane-1,3-dicarboxylic acid has been developed. TMCO exhibits high reactivity toward a number of carbenes and epoxidizing reagents, undergoing multiple cyclopropanations, dihalocyclopropanations, or epoxidations of four double bonds to yield polyspirocyclic products. Stereochemical features of polyspirocyclopropanated compounds have been thoroughly examined in experimental (NMR) and theoretical (DFT) studies. Comprehensive stereochemical assignment of TMCO adducts with dihalocarbenes and spiroepoxy products was achieved. The conditions of the formation of 1-methyl-3,7-bis(methylidene)bicyclo[3.3.1]-nonane from the adamantane derivative were optimized, and diadducts of this diene with dihalocarbenes were isolated and characterized.



INTRODUCTION

Three-membered rings, exemplified by cyclopropane and oxirane, are ubiquitous structural motifs present in a variety of natural products, biologically active molecules, and also in aesthetically appealing synthetic polycyclic and caged molecular architectures.[1] The interest in strained small polycycles encouraged broad and extensive studies focused on related problems, from existence and synthesis of highly strained compounds and fundamental aspects of bonding to conformational restriction of physiologically active compounds.[1−7] Among these particularly intriguing structures are cyclopropanes spiro-linked to a (poly)cyclic core. The compounds **1**−**3** with two spirocyclopropanes can be cited here as examples (Figure 1).[8−13] The structures possessing a central cyclic core exhaustively substituted by spirocyclopropanes were named rotanes (**4** and **5** in Figure 1).[11,14−16]

Although a variety of synthetic methods furnishing three-membered rings have been developed, the most general ones involve the formation of cyclopropane or oxirane rings from corresponding alkenes.[17] This is why the cyclic compounds outfitted with one or several exocyclic double bonds are the most practically useful starting materials for accessing structures of type **1**−**5**. This concept was applied in the synthesis of [4]-rotane from tetramethylenecyclobutane,[15] but other known [*n*]-rotanes were synthesized by various multistep methods because starting polyenes are not easily available. However, there are no general methods toward the synthesis of [*n*]-rotanes, and to date, their family is limited to [3]−[6]-rotanes.[1,14−16]

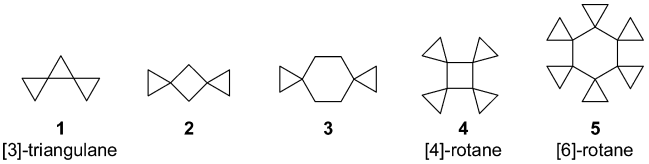


Figure 1. Examples of polyspirocycloalkanes and rotanes.

Here we report the synthesis of a series of pentacyclic polyspiro structures possessing an eight-membered aliphatic ring as a core fragment, starting from 1,3,5,7-tetrakis(methylidene)cyclooctane (**6**, TMCO) with four exocyclic double bonds.

RESULTS AND DISCUSSION

Synthetic Approach to TMCO. Synthesis of TMCO from 1,3-bis(bromomethyl)-5,7-dibromoadamantane (**7**, Scheme 1) was mentioned in a short communication[18] without an experimental procedure, and only a few reactions of TMCO with electrophilic reagents leading to the cross-cyclization back to the adamantane derivatives were briefly explored. However,

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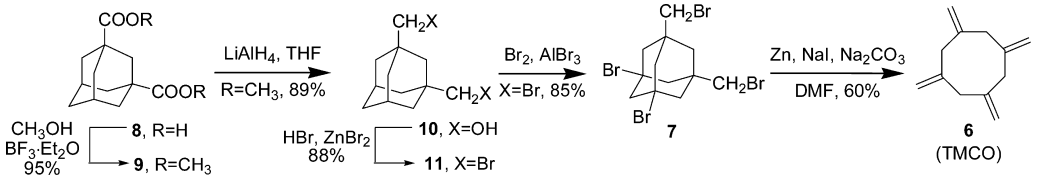
Scheme 1. Synthesis of TMCO from Adamantane-1,3-dicarboxylic Acid



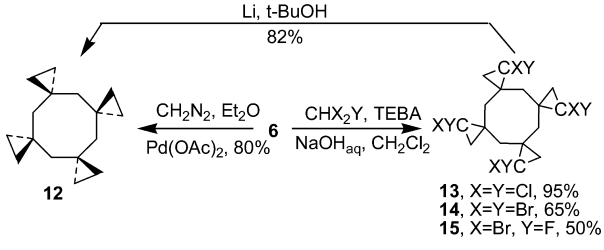
this work provided the correct structural assignment for TMCO, unlike the previously described attempt of TMCO synthesis via the tetramerization of allene, where the structure of *symm*-TMCO was incorrectly assigned to the nonsymmetric 1,2,4,7-tetrakis(methylidene)cyclooctane product.[19,20]

Another problem is that the starting tetrabromide **7** is not an easily accessible compound. Thus, in the present work, we report an optimized preparative method of the synthesis of TMCO and its subsequent cycloaddition reactions with carbenes and epoxidation leading to the novel polyspirocyclic structures of peculiar architecture.

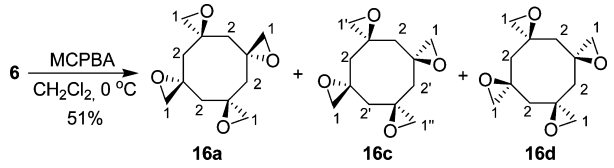
First, we have developed a practical and efficient protocol for the preparative five-step synthesis of TMCO (**6**) from commercial adamantane-1,3-dicarboxylic acid (**8**, Scheme 1). Although all precursors **7**–**11** were described, some of the procedures required considerable improvement and optimization. Direct reduction of dicarboxylic acid **8**[21−23] appeared to be complicated by its poor solubility in both THF and ether, which forced us to elaborate the two-step synthesis of diol **10** employing ester **9**. An attempt to obtain ester **9** from acid **8** using a reported procedure[24,25] through the corresponding chloroanhydride afforded exclusively 1,3-dichloroadamantane. On the contrary, the esterification of diacid **8** using boron trifluoride etherate proceeded in high yield, as well as the following reduction of diester **9**. Bromination of diol **10** with HBr−$ZnBr_2$ using a described method[21] was the only step that did not require any optimization, affording dibromide **11** as a sole product. Synthetic procedures for the preparation of tetrabromide **7** as well as for TMCO (**6**) were not documented,[18] compelling us to carefully optimize these steps. Tetrabromide **7** was obtained in a high yield by the treatment of compound **11** with excess of bromine in the presence of aluminum tribromide. The subsequent dehydrobromination along with fragmentation of the adamantane scaffold afforded TMCO in 60% yield. Thus, target tetraene **6** was obtained in 38% total yield.

Synthesis of Polyspirocyclic Compounds. The most interesting investigation of TMCO reactivity appeared to be the multiple cyclopropanation, dihalocyclopropanation, or epoxidation of its double bonds resulting in polyspirocyclic molecules **12**–**15** (Scheme 2) and **16** (Scheme 3). The treatment of TMCO with excess diazomethane in the presence of palladium(II) acetate gives only one product of complete cyclopropanation, an unusually stable pentacyclic hydrocarbon **12** in a high yield (Scheme 2).

Scheme 2. Synthesis of Polyspirocyclic Compounds from TMCO



Scheme 3. Synthesis and Stereochemistry of Tetraoxirane 16



The cycloaddition of dihalocarbenes to TMCO was carried out under phase transfer catalytic conditions. The reaction of TMCO with dichloro- or dibromocarbenes yielded tetra-adducts **13** or **14** in 95 and 65% yields, respectively, as a mixture of diastereomers (Scheme 2). The reduction of diastereomers **13** with lithium in *tert*-butanol afforded polyspirane **12** in a high yield (82%), which represents an alternative synthetic approach to this hydrocarbon.

For polyspirocyclic compounds **13** and **14**, four possible stereoisomers **a**–**d** with different orientations of the CX_2 fragment can exist (Figure 2). It is interesting that for both compounds **13** and **14** the preferential formation of isomer **d** with the arrangement of CX_2 groups at one face of the eight-membered cycle is observed (Figure 2).

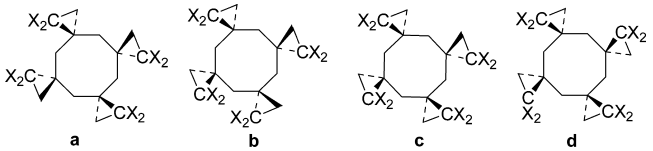


Figure 2. Possible stereoisomers of polyspirocyclic compounds **13** and **14**.

In order to study the stereochemistry of dihalocyclopropanation of TMCO, we attempted to separate the mixture of stereoisomers of tetra-adduct **13** using column chromatography, which allowed the isolation of two major isomers **13a** and **13d** as individual compounds in 15 and 46% yields, respectively. The minor isomers **13b** and **13c** were obtained only as a mixture in 2:5 ratio, 13% yield. Stereochemistry of **13a**–**d** was determined by ^1H and ^{13}C NMR.

In a fully symmetric averaged structure, diastereomer **13a** with an alternant steric arrangement of dichlorocyclopropane moieties in the molecule (D_{2d} point group symmetry)[26] should have only two types of equivalent protons: four CH_2 groups belonging to cyclopropanes and four CH_2 groups of the cyclooctane core, which would be revealed as two singlets in the ^1H NMR spectrum. While this was generally the case, the actual rate of conformational averaging at 25 °C was unexpectedly slow, as compared to much faster rates for reported cyclooctane derivatives,[27] resulting in a narrow singlet at 1.5 ppm for cyclopropane protons but a rather broad W =

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120 Hz signal at 2.22 ppm for the protons of the cyclooctane core. The low-temperature spectrum of **13a** in $CDCl_3$ (−61 °C) reveals two AB-systems: for the methylene protons of the eight-membered ring with a large difference of chemical shifts (1.18 and 3.16 ppm, J_{AB} = 16.2 Hz) and for the protons of the small rings (1.38 and 1.62 ppm, J_{AB} = 7.5 Hz). Increasing the temperature led to the line shape evolution for both AB-systems, typical of the two-site exchange. In the 59 °C spectrum, which corresponds to fast exchange, the width of the signal belonging to cyclooctane protons is 12 Hz (Figure 3).

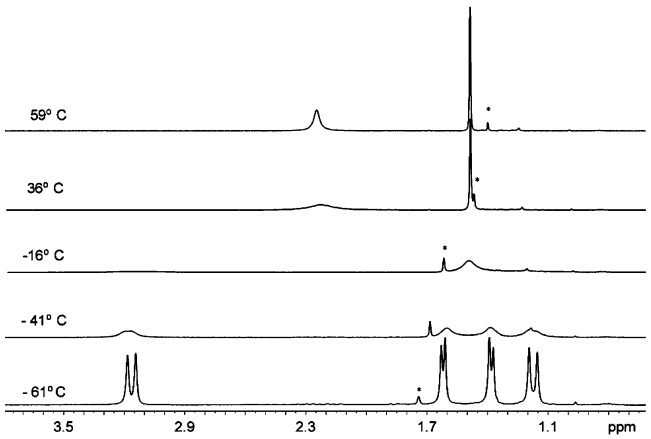


Figure 3. ^{1}H NMR spectra (400 MHz) of **13a** at various temperatures.

The evaluation of the rate constants k of the dynamic process[28] corresponds to the following activation parameters: $\Delta H^{\ddagger}$ = 10.8 ± 0.2 kcal/mol, $\Delta S^{\ddagger}$ = 7.3 ± 1.0 cal/mol·K, $\Delta G_{298}{}^{\ddagger}$ = 13.0 kcal/mol (see Supporting Information).

The ^{13}C NMR spectra of **13a** remained unchanged in the explored temperature range and contains only four signals, corresponding to the symmetrical structure with equivalent carbons. All the aforementioned NMR data are in a good agreement with DFT calculations, predicting the existence of **13a** mostly as the pair of energy-degenerate S_4-symmetric conformers (see the Conformational Analysis section).

Isomer **13b**, bearing two pairs of *anti*-oriented dichlorocyclopropanes and possessing a higher symmetry (C_{2h}) of the two minor diastereomers, is characterized by ^{1}H NMR spectra containing an AB-system of protons of all three-membered cycles with typical ^2J = 7.5 Hz and one singlet signal and one AB-system of two types of CH_2 groups of the cyclooctane ring. The ^{1}H NMR spectrum of isomer **13c** possessing three *syn*- and one *anti*-oriented cyclopropane ring (C_s) shows one AB-system from two equivalent cyclopropane moieties, two singlets from the other cyclopropanes, and two AB-systems from the protons of CH_2 groups of the eight-membered cycle. In the case of the last stereoisomer **13d** with all *syn*-orientation of cyclopropanes (C_{4v}), the protons of each methylene group of the eight-membered cycle are not equivalent and give a doublet typical of an AB-system with the characteristic constant ^2J = 16 Hz, while the sole singlet is observed for eight equivalent protons of the four cyclopropane rings. The ^{13}C NMR spectra of stereoisomers **13b−d** are also in agreement with the proposed configurations.

The dynamic ^{1}H NMR experiments showed that the components of both cyclooctane AB-systems of **13c** at −35 °C degenerated into broad signals, while the corresponding signals in the spectra of isomers **13b** and **13d** revealed only slight broadening in the explored temperature range.

Thus, we completed the stereochemical analysis and assignment of all possible isomers of tetra-adduct **13**, and these spectral criteria are applicable to octabromide **14**.

Notably, tetra-adduct **14** was obtained in lower yield (65%), presumably due to its decreased stability, and it was not possible to estimate the ratio of diastereomers in the reaction mixture in the presence of byproducts. After column chromatography, we isolated the major isomer **14d** in 41% yield. ^{1}H and ^{13}C NMR data confirmed the stereochemistry of this compound. The structure of **14d** was proved by X-ray analysis, and according to X-ray data, the cyclooctane scaffold in the crystal of molecule **14d** adopts "twisted chair-boat" conformation (see Supporting Information).[29,30]

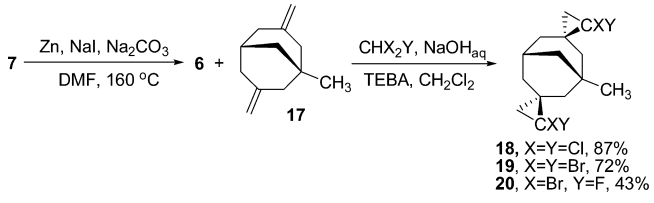
Earlier we reported that the *gem*-bromofluorocyclopropane moiety may behave differently in some processes, as compared with dibromo- or dichlorocyclopropane analogues.[31,32] Having this in mind, we studied the cycloaddition of bromofluorocarbene to TMCO and found that octahalogenide **15** was formed as an inseparable mixture of diastereomers in a moderate yield (Scheme 2).

Epoxidation of polymethylenecycloalkanes may offer a straightforward approach to unknown [*n*]-heterorotanes. In this respect, TMCO, containing four reactive exocyclic double bonds, represents a model compound for such a process. We studied the epoxidation of TMCO under classic conditions with *meta*-chloroperbenzoic acid (MCPBA) and found that the reaction proceeds smoothly, furnishing the corresponding tetraoxirane **16** in a high yield (Scheme 3). To the best of our knowledge, this is the first example of a system with more than two polyspiro-linked oxirane moieties on a cycloalkane scaffold.

Tetraoxirane **16** was formed as a mixture of three stereoisomers **16a−d** in a 5:3:1 ratio, which could not be separated by the column chromatography. The set of signals and their multiplicity in NMR spectra of diastereoisomers **16a−d** could be interpreted in a similar fashion, using the symmetry considerations developed for the corresponding diastereomers of octahalogenides **13** and **14**.

Synthesis of Diene 17 and the Products of Its Dihalocyclopropanation. When TMCO preparation from tetrabromide **7** was carried out in "reagent grade" DMF (i.e., not absolute) and commercial zinc dust without activation, these conditions led to the formation of a previously unknown diene, methyl-substituted bis(methylidene)bicyclononane **17** as an admixture to the target TMCO in **6**/**17** ratios from 10:1 to 1:1 (Scheme 4). Although our attempts to separate TMCO and diene **17** by preparative gas chromatography were not successful, the structure of **17** was proved by ^{1}H and ^{13}C NMR spectroscopy employing two-dimensional correlation techniques.

Scheme 4. Formation of Bis(methylene)bicyclononane 17 and the Products of Its Dihalocyclopropanation[33]



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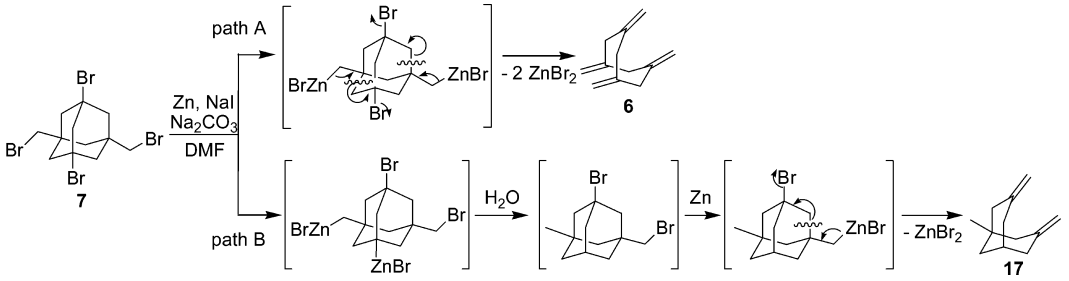
Scheme 5. Plausible Scheme of Formation of TMCO and Bis(methylene)bicyclononane 17



Considering the formation of diene **17** alongside with TMCO, we can speculate that, in this case, in parallel with the double fragmentation of the adamantane scaffold leading to TMCO (Scheme 5, path A), the mono fragmentation may prevail under the treatment of tetrabromide **9** with zinc due to the presence of traces of water as a proton source in the reaction mixture (Scheme 5, path B).

We converted the mixture of unsaturated hydrocarbons **6** and **17** into adducts with dihalocarbenes and managed to obtain compounds **18**, **19**, and **20** in pure form due to substantial differences in chromatographic mobilities for the octa- (**13**–**15**) and tetra- (**18**–**20**) halogenides (Scheme 4). The adducts of diene **17** with dichloro- and dibromocarbenes were obtained as one of three possible stereoisomers which are formed as a result of *exo*-addition of carbenes to the double bonds of the dual-chair bicyclo[3.3.1]nonane skeleton. The cycloaddition of bromofluorocarbene to diene **17** proceeded with the formation of a mixture of four diastereomers **20** with different orientations of fluorine toward the methyl group in the bicyclononane framework. The structures of compounds **18**–**20** were determined using ^{1}H and ^{13}C measurements and unambiguously proven by X-ray analysis of tetrachloride **18**.[30] As expected, in the crystalline state, the bicyclo[3.3.1]nonane scaffold of compound **18** existed in a double-chair conformation, which is in good agreement with X-ray data for the previously described product of dichlorocyclopropanation of bis(methylene)bicyclononane (see Supporting Information).[34−36]

Conformational Analysis. The structure of all-*syn* octabromide **14d** was unambiguously determined by X-ray analysis, which increased our confidence in the structural assignments of other compounds obtained in this study. However, we chose to augment the experimental data with theoretical calculations of ^{1}H NMR spectra, especially in view of the fact that some of the diastereomers described above were characterized as mixtures. In this work, we utilized a modified approach of Bally and Rablen,[37] which uses scaled Fermi contacts for calculating proton spin−spin coupling constants (SSCC). Specific details of this parametrization will be published elsewhere. The predicted spin−spin coupling constants matched the experimental values very well. Below, we report the detailed conformational analysis for isolated stereoisomers of octabromide **14d** and octachlorides **13a**–**d**; the data for the other compounds obtained in the course of the work are given in Supporting Information.

*Octabromide **14**.* The DFT structure of the lowest energy chair-boat conformer of all-*syn* **14d** closely resembled its X-ray structure, with the calculated geminal ^{2}J of 16.25 Hz nicely matching the observed value of 15.9 Hz. Linear correction of chemical shifts gave rmsd of 0.14 ppm. The conformational averaging is conceivably occurring via the slightly distorted (C_2) chair−chair conformer found at 2.7 kcal/mol (Figure 4).

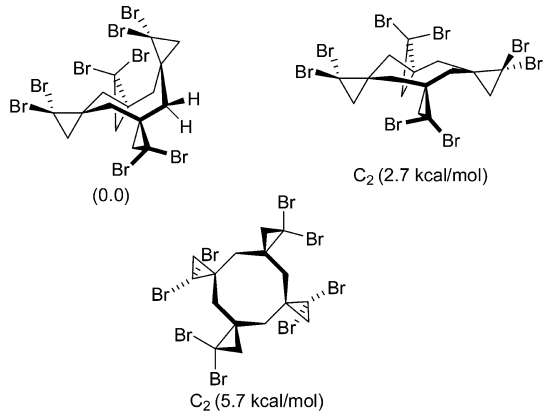


Figure 4. Low-energy conformers of octabromide **14d**.

A strongly twisted conformer possessing C_2-symmetry is 5.7 kcal/mol higher in energy. Interestingly, its geminal methylenic (cyclooctane) spin−spin coupling constants are computed at 16.7 and 16.9 Hz. Clearly, there is no reason to believe that this conformer is present in non-negligible quantities at equilibrium, as evidenced by both its high relative energy and a too large computed geminal SSCC.

*Octachlorides **13**.* The alternating isomer **13a** has two interconverting energy-degenerate S_4-symmetric conformers shown in Figure 5. The protons belonging to two types of methylene groups occupy symmetry-equivalent positions, so they are fully averaged into two singlets. The rate of interconversion is relatively slow, which is in accordance with the data of experimental dynamic NMR. The average chemical shifts for the two singlets were predicted with rmsd = 0.1 ppm.

The other conformers of **13a** are characterized with higher energies; the lowest one is 5 kcal/mol higher in energy than S_4 and can be neglected for NMR calculations. However, the higher energy conformers are relevant to the *mechanism* of unusually slow interconversion of the two mirror images of the low-lying S_4-symmetric conformer, shown in Figure 5, which we address here.

The major, lowest energy S_4-symmetric conformers seem to interconvert via the 5 kcal/mol asymmetric conformer (Figure 5b). The cyclooctane ring conversion from the *twisted boat-boat* to *chair-boat* conformation seems to be the rate-determining step for the overall conformational averaging in **13a**, with the transition state located at 10.9 kcal/mol (one imaginary frequency associated with the motion of the methylene identified with the red arrow).

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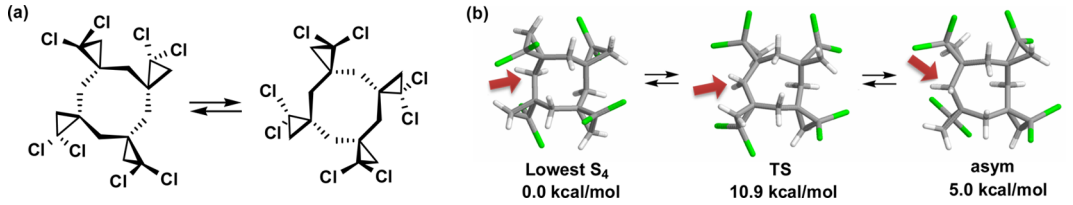

Figure 5. Two interconverting S_4-symmetric conformers of **13a** (a) and the potential rate-limiting step in the observed conformational averaging of **13a** (b).

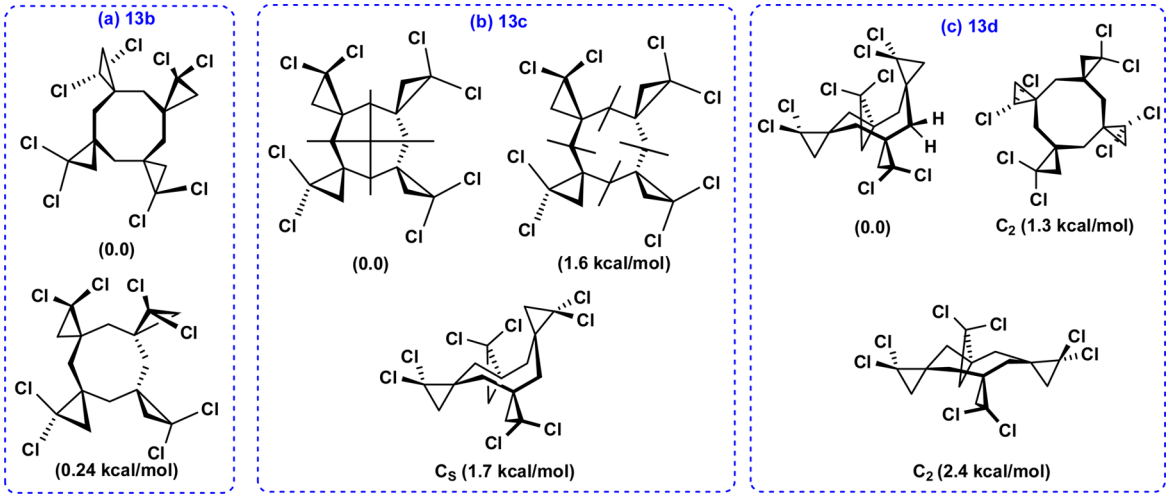

Figure 6. Low-energy conformers of octachlorides **13b–d**. Tilted lines in the 1.6 kcal/mol conformer of **13c** are shown to demonstrate some twisting of the cyclooctane core but not to indicate symmetry.

Since we could not unambiguously rule out an alternative lower energy path from the lowest S_4 to the higher lying S_4 conformers, it is possible that the step involving the 9.2 kcal/mol D_{2d}-symmetric transition state could be the rate-limiting step in the whole process of interconversion of the two enantiomeric low-energy conformers (see Supporting Information). However, this value is not in agreement with the result of the NMR experiment.

The less symmetric **13b**, which has an averaged apparent symmetry of C_{2h}, has two low-lying conformers, which are not symmetric at all (Figure 6a). At the B3LYP/6-311+G(d,p)//6-31G(d) level of theory, the conformers are nearly energy-degenerate. However, the difference of 0.2 kcal/mol is beyond the accuracy of this DFT method and should be taken with a grain of salt.

This is where computing the SSCCs and comparing them to the experimental values helps in determining which conformer is predominant. It is due to the fact that the spin–spin coupling constants, even the geminal ones, are very sensitive to the changes in geometry caused by the conformational equilibration. The calculated SSCCs for cyclopropyl methylenes were similar, slightly exceeding 8 Hz for both conformers (the experimental value is 7.6 Hz). However, the calculated values for the cyclooctane methylenes were different by more than 0.5 Hz. The experimental geminal cyclooctane constants in **13b** were measured at 16.2 Hz. Pairwise averaging of the calculated SSCCs for the slightly lower energy conformer (top in Figure 6a) gave 16.9 Hz, whereas the other conformer produced a much better calculated value of 16.3 Hz. While the small calculated DFT energy bias indicates that the top conformer of **13b** shown in Figure 6a is the major, based on the information derived from fitting of spin–spin coupling constants, it is likely that this conformer is in fact the minor component at the conformational equilibrium.

The least symmetric octachloride **13c** (apparent symmetry is C_s) had three relatively low-lying conformers shown in Figure 6. It is interesting that two of them are not symmetric, and only the third (at 1.7 kcal/mol) has a C_s-symmetric chair-boat conformation.

The calculated values for spin–spin coupling constants obtained by a proper averaging in all of these conformers deviated from the experimental values by more than 0.8 Hz, which did not allow an unambiguous stereochemical assignment. However, the experimental NMR is in good agreement with the C_s-symmetry of the proposed structure. Since the SSCCs for other isomers were predicted within the accuracy of 0.4–0.6 Hz or even better, we assert the structure of **13c** by ruling out the rest.

As it is with octabromide **14d**, the lower energy conformer of all-*syn* octachloride **13d** is also chair-boat (Figure 6c). However, unlike the bromide, the twisted "large boat" (C_2) conformer is lower in energy (1.3 kcal/mol) than the distorted (C_2) chair-chair conformer (2.4 kcal/mol). These two do not contribute to the NMR spectrum but plausibly serve as intermediates in the conformational averaging of the main chair-boat conformer, for which the only observed geminal constant, 15.9 Hz, matched the computed value of 16.32 Hz.

■ CONCLUSION

In conclusion, we have developed a convenient preparative method for the synthesis of a versatile synthone, tetraene **6**, with exocyclic double bonds—TMCO, and demonstrated its reactivity in epoxidation or [1 + 2]-cycloaddition reactions with a number of carbenes. Stereochemical features of polyspiro-

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cyclopropanated compounds have been thoroughly studied. TMCO has the potential to develop into a useful polyolefinic block, which could open ready access to novel highly strained polyspirocyclic structures.

EXPERIMENTAL SECTION

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a 400 MHz spectrometer (400.0, 100.6, and 376.3 MHz for ^{1}H, ^{13}C, and ^{19}F, respectively) at room temperature; chemical shifts δ were measured with a reference to the solvent for ^{1}H ($CDCl_3$, δ = 7.24 ppm) and ^{13}C ($CDCl_3$, δ = 77.13 ppm) and to $CFCl_3$ as an external standard for ^{19}F. Assignments of signals in the ^{1}H NMR spectra were made using COSY experiments and a spin simulation technique. Accurate mass measurements (HRMS) were obtained with electrospray ionization (ESI) and a time-of-flight (TOF) detector. Analytical thin layer chromatography was carried out with silica gel plates (supported on aluminum); the detection was done with a UV lamp (254 and 365 nm) and chemical staining (iodine vapor). Column chromatography was performed on silica gel (Merck, 230−400 mesh). All starting materials were commercially available. All reagents except commercial products of satisfactory quality were purified according to literature procedures prior to use.

Dimethyl Adamantane-1,3-dicarboxylate (9).[24,25] A mixture of adamantane-1,3-dicarboxylic acid (**8**) (4.92 g, 22 mmol), $BF_3{\cdot}Et_2O$ (6.25 g, 5.5 mL, 44 mmol), and CH_3OH (14.08 g, 18 mL, 440 mmol) was refluxed for 24 h. The reaction mixture was diluted with ether (30 mL) and treated with an aqueous solution of Na_2CO_3 (30 mL, 5 wt %). The organic layer was separated, and the water layer was extracted with ether (3 × 15 mL). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo to give **9**: Yield 5.34 g (95%), white solid, mp 51−53 °C; ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.55 (br s, 2H, 2CH), 1.72 (br dd, J = 12.5 Hz, J = 22.2 Hz, 8H, $4CH_2$), 1.89 (br s, 2H, CH_2), 2.02 (br s, 2H, CH_2), 3.53 (s, 6H, $2CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.7 (2CH), 35.3 (CH_2), 37.9 ($4CH_2$), 39.7 (2C), 40.8 (CH_2), 51.7 ($2CH_3$), 177.2 ($2CO_2$).

1,3-Bis(hydroxymethyl)adamantane (10).[22] A solution of dimethyl adamantane-1,3-dicarboxylate (**9**) (13.2 g, 52 mmol) in absolute THF (140 mL) was added dropwise to a suspension of $LiAlH_4$ (10.76 g, 283 mmol) in absolute THF (70 mL) for 30 min under argon to provide a gentle reflux of THF. The reaction mixture was refluxed for 3 h and cooled in the ice bath. Aqueous solution of NaOH (100 mL, 5 wt %) was added dropwise at 0 °C and the organic layer was separated by decantation. The solid residue was washed with THF (4 × 100 mL). The combined organic phases were concentrated in vacuo to give **10**: Yield 9.07 g (89%), white solid; mp 171−174 °C; ^{1}H NMR (400.0 MHz, DMSO-d_6) δ 1.13 (br s, 2H, 2CH), 1.32 (br d, J = 11.5 Hz, 4H, $4CH_2$), 1.40 (br d, J = 11.5 Hz, 4H, $4CH_2$), 1.53 (br s, 2H, CH_2), 1.97 (s, 2H, CH_2), 2.97 (br s, 4H, $2CH_2O$); ^{13}C NMR (100.6 MHz, $CDCl_3$/DMSO-d_6) δ 28.3 (2CH), 35.1 (2C), 37.0 (CH_2), 39.2 ($4CH_2$), 41.3 (CH_2), 72.4 ($2CH_2OH$).

1,3-Bis(bromomethyl)adamantane (11).[21] A mixture of diol **10** (3.00 g, 15 mmol) and HBr (52.5 mL, wt.-48%) was stirred for 10 min at room temperature. Then $ZnBr_2$ (17.4 g, 77 mmol) was added quickly. The reaction mixture was refluxed for 4 h and left overnight at room temperature. The solid residue was separated by decanting, washed with water (3 × 20 mL) and dried in the air to give **11**: Yield 4.25 g (88%), brown crystals, mp 84−85 °C; ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.39 (br s, 2H, 2CH), 1.50−1.54 (m, 8H, $4CH_2$), 1.57−1.61 (m, 2H, CH_2), 2.10−2.16 (m, 2H, CH_2), 3.21 (s, 4H, $2CH_2Br$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.6 (2CH), 34.4 (2C), 35.7 (CH_2), 39.9 ($4CH_2$), 43.7 (CH_2), 47.3 ($2CH_2Br$).

1,3-Dibromo-5,7-bis(bromomethyl)adamantane (7).[18] Bis-(bromomethyl)adamantane **11** (3.5 g, 10 mmol) was added to a solution of $AlBr_3$ (1.09 g, 4 mmol) in dry Br_2 (11 mL). The reaction mixture was refluxed for 25 h and then poured onto a mixture of ice (30 g) and Na_2SO_3 (30 g). The solid residue was filtered, washed with water (3 × 20 mL), and dried in the air to give **7**: Yield 4.08 g (85%), brown crystals, mp 153−155 °C; ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.50 (s, 2H, CH_2), 2.12 (dd, J = 12.6 Hz, J = 16.4 Hz, 8H, $4CH_2$), 2.72 (s, 2H, CH_2), 3.24 (s, 4H, $2CH_2Br$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 41.1 (CH_2), 41.3 (2C), 42.8 ($2CH_2Br$), 49.4 ($4CH_2$), 57.1 (CH_2), 58.8 (2CBr).

1,3,5,7-Tetrakis(methylidene)cyclooctane (6).[18] A solution of tetrabromide **7** (5.18 g, 10.8 mmol) in absolute DMF (15 mL) was added to a suspension of Zn dust (5.18 g, 80 mmol) activated with HCl,[38] Na_2CO_3 (8.29 g, 80 mmol), and NaI (0.26 g, 1.7 mmol) in absolute DMF (15 mL) at 160 °C while stirring. Simultaneously, TMCO (**6**) was distilled off with vapor of DMF from the reaction mixture. Then another portion of DMF (5 mL) was added to the reaction mixture and distilled off. The combined DMF fractions were diluted with water (45 mL) and extracted with pentane (3 × 10 mL). The combined pentane fractions were washed with water (3 × 10 mL), dried with $MgSO_4$, and concentrated in vacuo to give **6**: Yield 1.04 g (60%), colorless liquid, bp 40 °C (2 Torr); ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 2.88 (s, 8H, $4CH_2$), 4.82 (s, 8H, $4CH_2$═); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 44.1 ($4CH_2$), 113.8 ($4CH_2$═), 147.1 (4C═).

Tetraspiro[2.1.2^5.1.2^9.1.2^{13}.1^3]hexadecane (12). Method A: $Pd(OAc)_2$ (20 mg, 0.09 mmol) was added upon stirring to the solution of TMCO (150 mg, 0.9 mmol) in pentane (2 mL). The mixture was cooled to −4 °C, and the solution of diazomethane in ether (10 mL, 1 M) was added under vigorous stirring over 10 min. The mixture was filtered through a layer of silica gel and concentrated in vacuo to give **12**: Yield 0.16 g (80%), colorless liquid, R_f 0.75. **Method B**: Li (0.5 g, 71 mmol) was added in small portions during 96 h to the solution of octachloride **13** (550 mg, 1.1 mmol) in the mixture of *t*-BuOH (7 mL) and absolute ether (30 mL) under vigorous stirring and reflux under argon. The reaction mixture was quenched with water (50 mL) and extracted with ether (3 × 20 mL). The combined organic fractions were washed with water (3 × 10 mL), dried with $MgSO_4$, and concentrated in vacuo to give **12**: Yield 195 mg (82%); ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 0.24 (s, 16H, $8CH_2$, cy-Pr), 1.47 (s, 8H, $4CH_2$, cy-Oct); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.1 (J_{CH} = 161 Hz, $8CH_2$, cy-Pr), 18.6 ($4C_{spiro}$), 46.5 (J_{CH} = 125 Hz, $4CH_2$, cy-Oct). Anal. Calcd for $C_{16}H_{24}$: C, 88.82; H, 11.18. Found: C, 88.77; H, 11.38.

1,1,6,6,10,10,14,14-Octachlorotetraspiro-[2.1.2^5.1.2^9.1.2^{13}.1^3]hexadecane (13). A solution of NaOH (12 g, 300 mmol) in water (12 mL) was added dropwise to a vigorously stirred solution of TMCO (120 mg, 0.75 mmol) and TEBA (0.1 g, 0.4 mmol) in $CHCl_3$ (10 mL). The reaction mixture was stirred for 5 h at room temperature. Then it was diluted with CH_2Cl_2 (15 mL) and water (15 mL). The organic phase was separated and the water phase extracted with CH_2Cl_2 (3 × 10 mL). The combined organic fractions were washed with water (3 × 10 mL) and dried with $MgSO_4$. The solvent was evaporated in vacuo to give the mixture of isomers **13a−d** in a yield of 350 mg (95%). The mixture was separated by the column chromatography on silica gel, yielding **13a** (55 mg, 15%): white crystals, mp 160−162 °C, R_f 0.40 (petroleum ether); mixture of **13b** and **13c** (48 mg, 13%), colorless oil, R_f 0.45 (petroleum ether/EtOAc 20:1); and **13d** (170 mg, 46%), light-yellow crystals, mp 138−140 °C; R_f 0.38 (petroleum ether/EtOAc 20:1). **13a**: ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.50 s (8H, $4CH_2$, cy-Pr), 2.22 br s (line width ∼120 Hz, 8H, $4CH_2$, cy-Oct); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.0 ($4C_{spiro}$), 39.1 ($^1J_{CH}$ = 165 Hz, $4CH_2$, cy-Pr), 43.0 ($^1J_{CH}$ = 132 Hz, $4CH_2$, cy-Oct), 66.6 ($4CCl_2$). **13b**: ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.46 (d, 4H, J = 7.6 Hz, $4CH_2$, cy-Pr), 1.58 (d, 4H, J = 7.6 Hz, $4CH_2$, cy-Pr), 2.23 (d, 2H, J = 16.2 Hz, CH_2^8, CH_2^{16}), 2.33 (s, 4H, CH_2^4, CH_2^{12}), 2.62 (d, 2H, J = 16.2 Hz, CH_2^8, CH_2^{16}); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.6 ($4C_{spiro}$), 38.6 ($4CH_2$), 39.5 ($4CH_2$), 67.7 ($4CCl_2$). **13c**: ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.39 (d, 2H, J = 7.3 Hz, H^{7b}, H^{15b}), 1.46 (s, 2H, $2H^{11}$), 1.49 (d, 2H, J = 7.3 Hz, H^{7a}, H^{15a}), 1.57 s(s, 2H, $2H^2$), 2.13 (d, 2H, J = 16.1 Hz, H^{8b}, H^{12b}), 2.22 (d, 2H, J = 16.1, CH_2^4, CH_2^{16}), 2.34 (d, 2H, J = 16.1, CH_2^4, CH_2^{16}), 2.67 (d, 2H, J = 16.1, H^{8a}, H^{12a}); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 30.5 (CH_2^{11}), 30.7 (C^9), 30.9 (C^3), 31.4 (C^5, C^{13}), 35.86 (CH_2^7, CH_2^{15}), 35.91 (CH_2^2), 39.4 (CH_2^8, CH_2^{12}), 40.9 (CH_2^4, CH_2^{16}), 65.89 (CCl_2^6, CCl_2^{14}), 67.38 (CCl_2^{10}), 69.37 (CCl_2^1). **13d**: ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.41 (s, 8H, $4CH_2$, cy-Pr), 2.06 (d, 4H, $^2J_{HH}$ = 15.9 Hz, $4CH_2$, cy-Oct), 2.69 (d, 4H, $^2J_{HH}$ = 15.9 Hz, $4CH_2$, cy-Oct); ^{13}C NMR (100.6 MHz,

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$CDCl_3$) δ 30.9 ($4C_{spiro}$), 32.4 ($^1J_{CH}$ 161 Hz, $4CH_2$, cy-Pr), 39.4 ($^1J_{CH}$ 130 Hz, $4CH_2$, cy-Oct), 67.4 ($4CCl_2$). Anal. Calcd for $C_{16}H_{16}Cl_8$: C, 39.02; H, 3.25. Found for **13a–d**: C, 39.07; H, 3.32.

1,1,6,6,10,10,14,14-Octabromotetraspiro-[2.1.2^5.1.2^9.1.2^{13}.1^3]hexadecane (14). TMCO (0.15 g, 0.9 mmol) and finely powdered KOH (0.61 g, 11 mmol) were added to a vigorously stirred solution of TEBA (0.01 g, 0.04 mmol) and $CHBr_3$ (1.01 g, 0.3 mL, 4 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The reaction mixture was stirred for 4 h at 0 °C and filtered through a layer of silica gel. The solvent was evaporated in vacuo to give the residue **14a–d**: Yield 495 mg (65%). The separation by the column chromatography on silica gel afforded **14d**: Yield 310 mg (41%), light-yellow crystals, mp 186–188 °C, R_f 0.30 (petroleum ether/EtOAc 20:1); ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.61 (s, 8H, $4CH_2$, cy-Pr), 2.17 (d, J = 15.9 Hz, 4H, $4CH_2$, cy-Oct), 2.86 (d, J = 15.9 Hz, 4H, $4CH_2$, cy-Oct); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 30.0 ($4C_{spiro}$), 34.5 ($^1J_{CH}$ = 164 Hz, $4CH_2$, cy-Pr), 44.0 ($^1J_{CH}$ = 130 Hz, $4CH_2$, cy-Oct), 39.2 ($4CBr_2$). Anal. Calcd for $C_{16}H_{16}Br_8$: C, 22.64; H, 1.89. Found: C, 22.65; H, 1.97.

1,6,10,14-Tetrabromo-1,6,10,14-tetrafluorotetraspiro-[2.1.2^5.1.2^9.1.2^{13}.1^3]hexadecane (15). An aqueous solution of NaOH (4 mL, 50 wt %) was added dropwise to a stirred mixture of TMCO (100 mg, 0.6 mmol), $CHBr_2F$ (1.44 g, 7.5 mmol), and TEBA (4 mg, 0.05 mmol) in CH_2Cl_2 (4 mL) at 0 °C. The reaction mixture was warmed up to room temperature and stirred for 120 h. Then it was diluted with CH_2Cl_2 (5 mL) and treated with ice water (5 mL). The organic phase was separated and the water phase extracted with CH_2Cl_2 (3 × 5 mL). The combined organic fractions were washed with water (3 × 5 mL) and dried with $MgSO_4$. The solvent was evaporated in vacuo; the residue was purified by column chromatography on silica gel to give mixture of diastereomers **15**: Yield 180 mg (50%), colorless oil, R_f 0.40 (petroleum ether/EtOAc 10:1.5); ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.09–1.35 (m), 1.38–1.58 (m), 1.66–1.81 (m), 1.95–2.05 (m), 2.09–2.18 (m), 2.40–2.66 (m); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.7 (J_{CF} = 10 Hz), 27.0 (J_{CF} = 10 Hz), 27.2 (J_{CF} = 10 Hz), 27.8 (J_{CF} = 10 Hz), 28.4 (J_{CF} = 10 Hz), 28.6 (J_{CF} = 10 Hz), 28.7–29.2 (m), 29.7, 29.9, 30.3, 30.4, 30.5, 31.1, 31.2, 31.3, 32.4, 32.5, 32.6, 36.1, 36.2, 36.5, 36.6, 37.5, 37.6, 38.9, 39.1, 42.0, 42.4, 42.7, 43.8, 45.1, 88.26 (J_{CF} = 305 Hz), 88.29 (J_{CF} = 305 Hz), 88.3 (J_{CF} = 305 Hz), 88.4 (J_{CF} = 304 Hz), 88.5 (J_{CF} = 304 Hz), 88.6 (J_{CF} = 300 Hz), 89.2 (J_{CF} = 301 Hz), 89.2 (J_{CF} = 303 Hz), 90.2 (J_{CF} = 303 Hz); ^{19}F NMR (367.0 MHz, $CDCl_3$) δ −136.00 to −135.87 (m, 1 isomer), −135.63 to −135.44 (m, 3 isomers), −135.39 (dd, J_{HF} = 8.9 Hz, J_{HF} = 17.9 Hz, 1 isomer), −135.30 to −135.13 (m, 1 isomer), −134.63 (dd, J_{HF} = 8.8 Hz, J_{HF} = 18.5 Hz, 1 isomer), −134.54 (dd, J_{HF} = 9.5 Hz, J_{HF} = 18.5 Hz, 1 isomer), −134.26 (dd, J_{HF} = 9.3 Hz, J_{HF} = 18.5 Hz, 1 isomer). Anal. Calcd for $C_{16}H_{16}Br_4F_4$: C, 31.82; H, 2.67. Found: C, 32.07; H, 2.86.

1,6,10,14-Tetraoxatetraspiro[2.1.2^5.1.2^9.1.2^{13}.1^3]hexadecane (16). MCPBA (570 mg, 3.3 mmol) was added to the solution of TMCO (110 mg, 0.69 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and for 2 h at room temperature. Then it was quenched with a solution of Na_2SO_3 (10 mL, 10 wt %) and saturated solution of Na_2CO_3 (10 mL). The organic phase was separated and the water phase extracted with CH_2Cl_2 (2 × 10 mL). The combined organic fractions were washed with water (2 × 5 mL) and dried with $MgSO_4$. The solvent was evaporated in vacuo; the residue was purified by the column chromatography on silica gel to give mixture of diastereomers **16a–d** in a 1.4:1:2 ratio: Yield 78 mg (51%), colorless crystals; mp 126–128 °C, R_f 0.42 ($CH_3OH/CHCl_3$ 1:20). **16a**: ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.99 (s, 8H, $4CH_2$, cy-Oct), 2.76 (s, 8H, $4CH_2O$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 42.8 (J_{CH} = 128 Hz, $4CH_2$, cy-Oct), 53.9 (J_{CH} = 175 Hz, $4CH_2O$), 55.0 (4C). **16c**: ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.41 (d, J = 14.9 Hz, 2H, $2CH_2$, cy-Oct), 1.75 (d, J = 14.9 Hz, 2H, $2CH_2$, cy-Oct), 2.12 (d, J = 14.7 Hz, 2H, $2CH_2$, cy-Oct), 2.63 (d-like, J = 5.1 Hz, 2H, $2CH_2O$), 2.667 (s, 2H, CH_2O), 2.673 (s, 2H, CH_2O), 2.73 (d, J = 14.9 Hz, 2H, $2CH_2$, cy-Oct), 3.02 (d-like, J = 5.1 Hz, 2H, $2CH_2O$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 41.9 (J_{CH} = 130, $2CH_2$, cy-Oct), 43.2 (J_{CH} = 128 Hz, $2CH_2$, cy-Oct), 52.6 (CH_2O), 53.3 (J_{CH} = 175 Hz, $2CH_2O$), 53.8 (J_{CH} = 175 Hz, CH_2O), 54.6 (C), 55.6 (2C), 56.0 (C). **16d**: ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.49 (d, J = 14.6 Hz, 4H, $4CH_2$, cy-Oct), 2.56 (d, J = 14.6 Hz, 4H, $4CH_2$, cy-Oct), 2.57 (s, 8H, $4CH_2O$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 42.6 ($4CH_2$, cy-Oct), 53.2 (J_{CH} = 175 Hz, $4CH_2O$), 55.2 (4C); HRMS calcd for $C_{12}H_{16}O_4$ $[M + Na]^+$ 247.0941, found 247.0938. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.29; H, 7.14. Found for a mixture of **16a–d**: C, 64.30; H, 7.28.

Synthesis of Tetrahalogenides 18–20. 1-Methyl-3,7-bis-(methylidene)bicyclo[3.3.1]nonane (**17**) was obtained from tetrabromide **7** (4.80 g, 10.0 mmol) according to the same procedure as described for TMCO when using commercial DMF and commercial nonactivated Zn dust. Diene **17** was isolated as a mixture with TMCO in 1:1 molar ratio: Yield of the mixture 0.74 g; resulting mixture was employed in the reactions of dihalocyclopropanation; ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 0.90 (s, 3H, CH_3), 1.47 (m, 2H, CH_2^9), 1.99 (d, 2H, J = 14.4 Hz, CH_2^2, CH_2^8), 2.07 (m, 1H, CH), 2.18 (d, 2H, J = 14.4 Hz, CH_2^2, CH_2^8), 2.27 (dd, 4H, J = 14.4 Hz, J = 5.1 Hz, CH_2^4, CH_2^6), 4.51 (ddd, J = 2.3 Hz, J = 2.3 Hz, J = 2.3 Hz, 2H, $2CH_2$=), 4.53 (ddd, J = 2.3 Hz, J = 2.3 Hz, J = 2.3 Hz, 2H, $2CH_2$=); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 29.7 (CH), 31.5 (C^1), 31.7 (CH_3), 39.9 ($2CH_2$), 40.9 (CH_2^9), 47.7 ($2CH_2$), 109.8 ($2CH_2$=), 145.6 (2C=).

(1*R*,1′*s*,5′*r*,7″*S*)-2,2,2″,2″-Tetrachloro-1′-methyldispiro-[cyclopropane-1,3′-bicyclo[3.3.1]nonane-7′,1″-cyclopropane] (18). Compound **18** was obtained according to the same procedure as octachloride **13** from diene **17** (122 mg, 0.75 mmol) and isolated by preparative column chromatography on silica gel: Yield 214 mg (87%),[33] white crystals, mp 114–115 °C, R_f 0.1 (petroleum ether); ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 0.99 (s, 3H, CH_3), 1.15 (d, 2H, J = 14.2 Hz, $H^{2'a}$, $H^{8'a}$), 1.28 (d, 2H, J = 14.2 Hz, $H^{4'b}$, $H^{6'b}$), 1.34 (d, 2H, J = 7.1 Hz, $2CH_2$, cy-Pr), 1.35 (d, 2H, J = 7.1 Hz, $2CH_2$, cy-Pr), 1.43 (m, 2H, $CH_2^{9'}$), 1.89 (d, 2H, J = 14.2 Hz, $H^{2'b}$, $H^{8'b}$), 2.17 (dd, 2H, J = 14.2 Hz, J = 5.4 Hz, $H^{4'a}$, $H^{6'a}$), 2.35 (ttt, 1H, J = 5.4 Hz, J = 3.2 Hz, J = 2.4 Hz, $CH^{5'}$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.9 ($2C_{spiro}$), 29.6 ($^1J_{CH}$ = 130 Hz, CH), 31.3 ($C^{1'}$), 32.3 ($^1J_{CH}$ = 125 Hz, CH_3), 37.6 ($^1J_{CH}$ = 162 Hz, $2CH_2$, cy-Pr), 38.3 ($^1J_{CH}$ = 128 Hz, $CH_2^{4'}$, $CH_2^{6'}$), 39.0 ($^1J_{CH}$ = 125 Hz, $CH_2^{9'}$), 45.6 ($^1J_{CH}$ = 128 Hz, $CH_2^{2'}$, $CH_2^{8'}$), 67.2 ($2CCl_2$).

(1*R*,1′*s*,5′*r*,7″*S*)-2,2,2″,2″-Tetrabromo-1′-methyldispiro-[cyclopropane-1,3′-bicyclo[3.3.1]nonane-7′,1″-cyclopropane] (19). Compound **19** was obtained according to the same procedure as octabromide **14** from diene **17** (122 mg, 0.75 mmol) and isolated by preparative column chromatography on silica gel: Yield 273 mg (72%),[33] white crystals, mp 154–156 °C, R_f 0.1 (petroleum ether); ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 1.05 (s, 3H, CH_3), 1.22 (d, 2H, J = 14.1 Hz, $H^{2'a}$, $H^{8'a}$), 1.35 (d, 2H, J = 14.1 Hz, $H^{4'b}$, $H^{6'b}$), 1.44 (m, 2H, $CH_2^{9'}$), 1.62 (d, 2H, J 7.3 Hz, $2CH_2$, cy-Pr), 1.63 (d, 2H, J = 7.3 Hz, $2CH_2$, cy-Pr), 1.91 (d, 2H, J = 14.1 Hz, $H^{2'b}$, $H^{8'b}$), 2.20 (dd, 2H, J = 14.1 Hz, J = 5.4 Hz, $H^{4'a}$, $H^{6'a}$), 2.37 (ttt, 1H, J = 5.4 Hz, J = 3.3 Hz, J = 2.3 Hz, $CH^{5'}$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.8 ($2C_{spiro}$), 30.4 (CH), 32.1 ($C^{1'}$), 32.2 (CH_3), 39.0 ($CH_2^{9'}$), 39.7($2CBr_2$), 40.2 ($2CH_2$, cy-Pr), 40.8 ($CH_2^{4'}$, $CH_2^{6'}$), 47.8 ($CH_2^{2'}$, $CH_2^{8'}$). Anal. Calcd for $C_{14}H_{18}Br_4$: C, 33.24; H, 3.59. Found: C, 33.53; H, 3.77.

(1′*s*,5′*s*)-2,2″-Dibromo-2,2″-difluoro-1′-methyldispiro[cyclopropane-1,3′-bicyclo[3.3.1]nonane-7′,1″-cyclopropane] (20). Compound **20** was obtained according to the same procedure as octahalogenide **15** from diene **17** (122 mg, 0.75 mmol) and isolated by preparative column chromatography on silica gel: Yield 123 mg (43%),[33] colorless oil, R_f 0.1 (petroleum ether); ^{1}H NMR (400.0 MHz, $CDCl_3$) δ 0.96 (s, 3H, CH_3), 0.97 (s, 6H, $2CH_3$), 0.98 (s, 3H, CH_3), 1.00–1.09 (m, 4H, CH_2, cy-Hex), 1.12–1.21 (m, 4H, CH_2, cy-Hex), 1.13–1.23 (m, 8H, $2CH_2$, cy-Pr), 1.14–1.24 (m, 4H, CH_2, cy-Hex), 1.24–1.33 (m, 4H, CH_2, cy-Hex), 1.36–1.50 (m, 8H, $2CH_2$, cy-Pr), 1.42 (m, 8H, CH_2, bridge), 1.73–1.77 (m, 4H, CH_2, cy-Hex), 1.77–1.82 (m, 4H, CH_2, cy-Hex), 2.02–2.08 (m, 4H, CH_2, cy-Hex), 2.04–2.11(m, 4H, CH_2, cy-Hex), 2.28 (m, 4H, CH, bridge); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.35 (J_{CF} = 8.7 Hz, $2C_{spiro}$), 26.36 (J_{CF} = 8.7 Hz, $2C_{spiro}$), 26.43 (J_{CF} = 8.7 Hz, $2C_{spiro}$), 26.44 (J_{CF} = 8.7 Hz, $2C_{spiro}$), 28.2 (J_{CH} = 133 Hz, CH), 28.6 (J_{CH} = 133 Hz, 2CH), 29.8 (C, bridge), 30.2 (2C, bridge), 30.60 (J_{CH} = 133 Hz, CH), 30.61(C, bridge), 32.19 (J_{CH} = 126 Hz, CH_3), 32.22 (J_{CH} = 126 Hz, $2CH_3$), 32.25 (J_{CH} = 126

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Hz, CH_3), 33.71 (J_{CH} = 160 Hz, J_{CF} = 8.7 Hz, $2CH_2$, cy-Pr), 33.73 (J_{CH} = 160 Hz, J_{CF} = 8.7 Hz, $2CH_2$, cy-Pr), 33.90 (J_{CH} = 160 Hz, J_{CF} = 8.7 Hz, $2CH_2$, cy-Pr), 33.91 (J_{CH} = 160 Hz, J_{CF} = 8.7 Hz, $4CH_2$, cy-Pr), 34.26 (J_{CH} = 129 Hz, J_{CF} = 8.3 Hz, $2CH_2$, cy-Hex), 34.30 (J_{CH} = 129 Hz, J_{CF} = 8.3 Hz, $2CH_2$, cy-Hex), 39.19 (J_{CH} = 130 Hz, CH_2, bridge), 39.23 (J_{CH} = 130 Hz, CH_2, bridge), 39.28 (J_{CH} = 130 Hz, CH_2, bridge), 39.75 (J_{CH} = 129 Hz, J_{CF} = 2.2 Hz, $2CH_2$, cy-Hex), 39.81 (J_{CH} = 129 Hz, J_{CF} = 2.2 Hz, $2CH_2$, cy-Hex), 41.48 (J_{CH} = 126 Hz, J_{CF} = 7.7 Hz, $2CH_2$, cy-Hex), 41.49 (J_{CH} = 126 Hz, J_{CF} = 7.7 Hz, $2CH_2$, cy-Hex), 47.18 (J_{CH} = 126 Hz, J_{CF} = 2.0 Hz, $2CH_2$, cy-Hex), 47.20 (J_{CH} = 126 Hz, J_{CF} = 2.0 Hz, $2CH_2$, cy-Hex), 90.47 (J_{CF} = 301.5 Hz, 4BrCF), 90.54 (J_{CF} = 301.5 Hz, 4BrCF); ^{19}F NMR (367.0 MHz, $CDCl_3$) δ −139.54 to −139.27 (m, 8F), −139.08 to −138.94 (m, 8F). Anal. Calcd for $C_{14}H_{18}Br_2F_2$: C, 43.78; H, 4.72. Found: C, 44.14; H, 4.99.

■ ASSOCIATED CONTENT

Supporting Information

X-ray data for compounds **14d** and **18**. The calculation of activation parameters for compound **13a**. Copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra of the reported compounds. Conformational analysis and NMR calculations for compounds **13a** and **16**−**19**. Computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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